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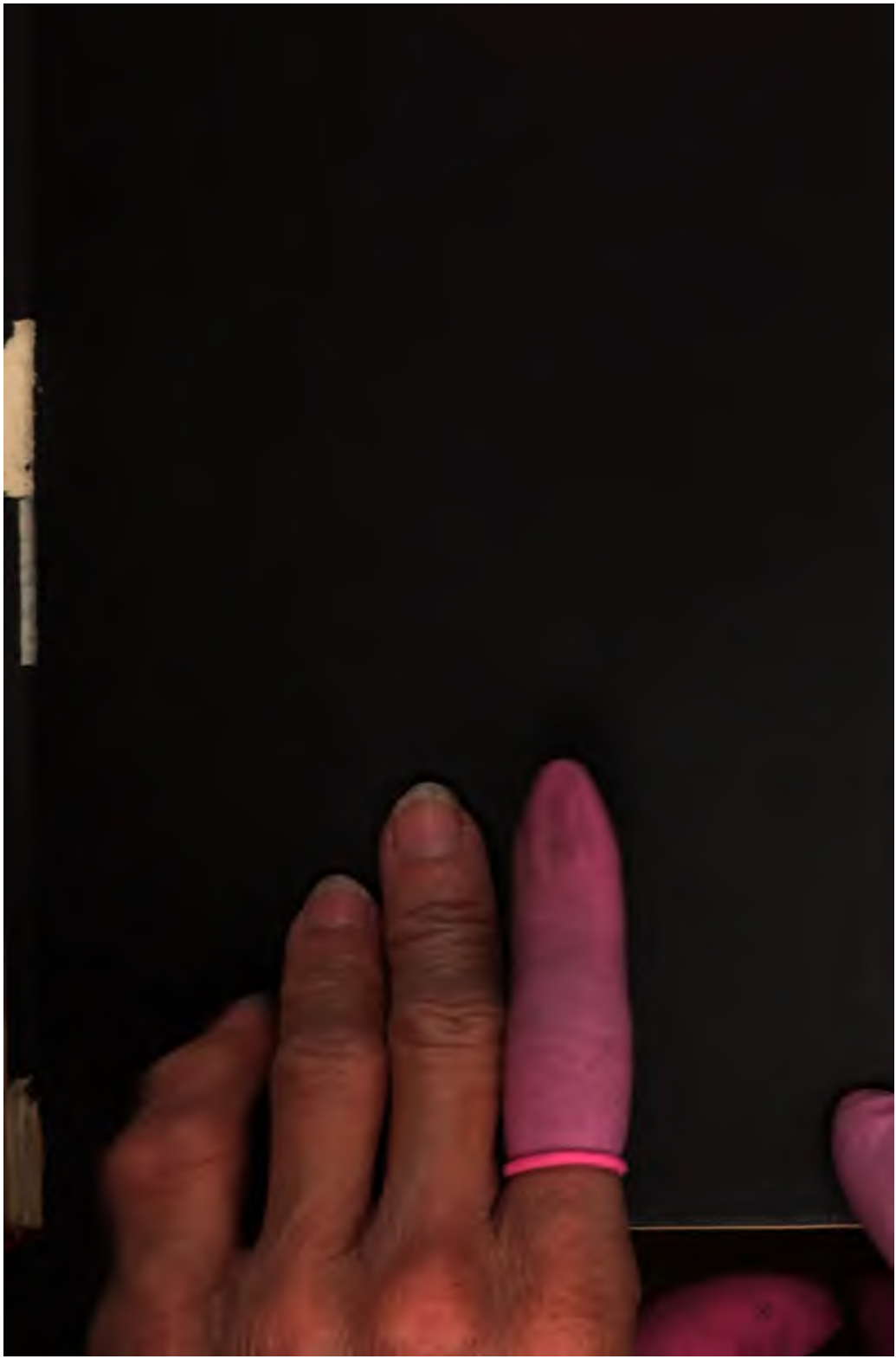

LECTURES ON
RENAL AND URINARY DISEASES.

LECTURES

ON

RENAL & URINARY DISEASES.

BY

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PREFACE.

THE favour accorded to these lectures has induced me to re-publish them in a single volume. They have been carefully revised, much new matter has been added to them, and I have included a fourth section on miscellaneous affections of the kidney, which makes the book more complete as a work of reference.

R. S.

BIRMINGHAM, *September, 1896.*

PREFACE TO THE FIRST EDITION OF THE LECTURES ON BRIGHT'S DISEASE.

In presenting this work for the indulgent consideration of my professional readers, I would disclaim all pretension to have said the last word on the many vexed questions with which its subject matter is encumbered. I have endeavoured to explain, within a modest compass, the present state of contemporary knowledge, making such additions and suggestions as have resulted from thirteen years' clinical and pathological study of *Bright's Disease*. Some of the material for this book has been previously published, but every chapter has been re-written, every point has been thought out again, and I need offer no apology for such alterations of opinion as may be perceptible in these pages.

Except where the source is acknowledged, all the figures have been drawn by myself from preparations in my possession. I desire to express my indebtedness to Dr. G. F. Crooke, Pathologist to the General Hospital, for many beautiful microscopical preparations; to Dr. MacMunn, and Mr. Eales, for kindly overlooking portions of the proof-sheets; to the publishers of Landois and Stirling's Physiology for

permission to use certain illustrations of the Anatomy of the Kidney; and to all preceding writers on Urinary Disease, among whom I desire to mention SIR WILLIAM ROBERTS, whose work on Urinary and Renal Diseases must remain for all time a never-failing source of sound clinical information.

R. S.

BIRMINGHAM, *February, 1889.*

PREFACE TO THE FIRST EDITION OF THE LECTURES ON DIABETES.

THE very kind reception accorded to my "Lectures on Bright's Disease," has encouraged me to publish the present volume.

These Lectures have, in great part, appeared already in print, but, with the exception of the Bradshaw Lecture, which is reproduced *verbatim*, they have undergone considerable modifications.

I desire to express my grateful thanks to the Right Hon. LORD KNUTSFORD, G.C.M.G., Her Majesty's Secretary of State for the Colonies, for the valuable assistance he has afforded me by obtaining for me a return showing the incidence of Diabetes Mellitus in the British Colonies.

I wish to acknowledge my indebtedness to many successive pathologists, resident medical officers and

clinical clerks at the General Hospital, for their indispensable co-operation in these pathological and clinical studies, and I desire to thank my friend, Mr. GILBERT BARLING, for his kindness in helping me to see this book through the press.

R. S.

BIRMINGHAM, *January, 1891.*

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LECTURES ON
RENAL AND URINARY DISEASES.

SECTION I.—BRIGHT'S DISEASE.

CHAPTER I.

GENERAL ANATOMY OF THE KIDNEY.

THE shape of the kidney, in health, is a flattened ovoid, larger and rounded above, flattened and pointed below. Its colour is dark-red with a smooth surface. The average length is 4·4 inches, the breadth two inches, and the thickness one inch.

The usual weight is about five and a half ounces in the male, and five ounces in the female. At the end of this chapter a table of weights at different ages is appended. The outer border is convex and rounded, while the inner is concave and traversed by a longitudinal fissure,—the *hilum*, in which are situated the renal vein, ureter, and renal artery. The hilum leads into a hollow in the kidney called the *sinus*, in which the vessels lie before penetrating the renal substance.

The kidney is enveloped by a thin tough fibrous capsule, which is continuous with the outer fibrous coat of the ureter. This capsule is attached to the renal substance by fine processes of connective tissue and by blood vessels.

Under the capsule there is a layer of un-striped muscular fibres.

On section the kidney is seen to be made up of two portions: (1,) an outer light brown portion, the *cortical layer*, of friable consistence and fairly homogeneous appearance ; and, (2,) an inner darker portion composed of a series of cones, the pyramids of Malpighi, whose apices are turned towards the sinus, the *medullary layer*. This inner layer is divided by

anatomists into two parts, — a *boundary zone* consisting of the broader portions of the pyramids, and a *papillary portion*, constituted by the projecting apices.

The relative proportions of these three divisions are, according to Klein,

Cortical Layer - - - - - -	3·5
Boundary Zone - - - - - -	2·5
Papillary Portion - - - - - -	4·0

The structure of the cortex is slightly granular from the presence of the Malpighian bodies, while it is marked by lighter lines at right angles to its surface.

The *medullary rays*, or pyramids of Ferrein, are conical bundles of straight tubules running from the cortex into the medulla.

Between the medullary rays are the interlobular vessels, the Malpighian bodies, and the convoluted tubules, together forming the *labyrinth*.

The medulla is distinctly striated by alternating light and dark lines arranged fan-wise, the handles of the fans being at the apices of the pyramids. The whitish lines are bundles of straight tubes, the darker lines blood vessels.

In the fœtus the kidney is distinctly lobulated, each lobule consisting of a pyramid of Malpighi with its corresponding cortical portion. In the adult this lobulated condition persists only rarely, but the connection between each pyramid and the uriniferous tubules and blood vessels of its cortical portion always remains (*Fig.* 3).

The *uriniferous tubules* take origin in Bowman's capsules, membranous expansions of their extremities, measuring $\frac{1}{250}$ of an inch in diameter. They pursue a tortuous course, effect junctions with one another, and ultimately form large collecting tubes which open on the apices of the papillæ. Each tubule is formed of a homogeneous basement membrane lined by epithelial cells, with an axial space or lumen for the passage of urine.

Fig. 1 represents the course of a uriniferous tubule. Connected by a narrow neck (2) with Bowman's capsule (1) is the *proximal convoluted tubule* (3), which ultimately leaves the labyrinth and passes down the medullary ray into a pyramid. Before leaving the labyrinth its convoluted appearance becomes less pronounced, and it is called a *spiral tubule* (4); descending, it narrows very much, finally turning at Henle's loop (6), the descending and ascending portions being called

the *descending* and *ascending limbs of Henle's looped tube.* The ascending limb is at first spiral, then wavy, and on reaching the cortex it re-enters the labyrinth as an *irregular tubule* (10),—a short irregular portion, which soon becomes wide and

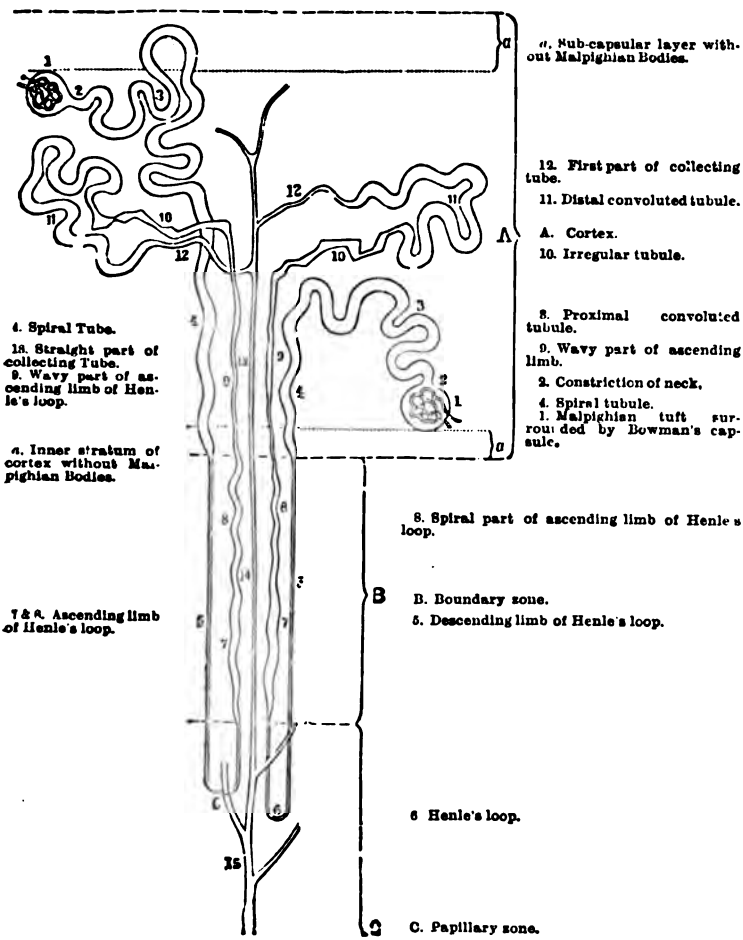

Fig. 1.—Diagram of course of two urinary tubules (after Landois and Stirling).

convoluted, forming the *distal convoluted tubule* (11), which after pursuing a tortuous course again enters a medullary ray as a *collecting tube* (12); this collecting tube passes down into

a pyramid, is joined by others and opens on the surface of the apex of a papilla.

The convoluted tubules are lined by a large granular epithelium arranged in a single layer. The cells are composed of two parts, an inner containing a spherical nucleus, and an outer part which has a fibrillated appearance from the presence of rods placed at right angles to the axis of the tube.

The cells appear continuous, no separation between them being ordinarily visible, adjacent cells interlocking by tooth-like projections on their surfaces.

Similar epithelium is found in the *spiral tubule*, and the *ascending limb* of Henle's loop.

In the *descending limb* the epithelium is clear and flattened with a bulging nucleus.

In the *irregular tubule* the cells somewhat resemble those of the convoluted tubes, but they are shorter, the nuclei are oval and the rods are coarser and better defined.

The *collecting tubes* are lined by large clear cubical or columnar epithelium with distinct nuclei.

Malpighian bodies are small spherical structures composed of Bowman's capsules, already alluded to, which enclose capillary tufts, and are pierced by *afferent* and *efferent* vessels. They are situated upon the extremities of horizontal branches of the interlobular arteries, and are about $\frac{1}{250}$ of an inch in diameter. Within the capsule each afferent vessel breaks up to form a capillary tuft, an arrangement of vascular loops supported by connective tissue and covered by a layer of endothelium (*Fig.* 2, GL).

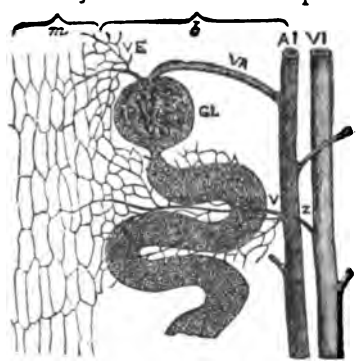

Fig. 2.—Diagram of arrangement of blood vessels in the renal cortex (after Tyson). *m*, region of the medullary ray; *b*, region of the convoluted tubules; VI, interlobular vein; AI, interlobular artery; VA, vas afferens; VE, vas efferens; GL, Bowman's capsule containing capillary tuft; VZ, venous radicle of interlobular vein.

The inner surface of the capsule is likewise covered by a lining of flattened cells, which are continuous with and probably modifications of the tubular epithelium.

Blood vessels. — The renal artery as it enters the hilum divides into four or five branches, which are invested by sheaths derived from the fibrous capsule. They pass in-

wards between the bases of the papillæ to form arches with one another in the boundary zone.

From these arches the *interlobular arteries* arise; they ascend towards the surface of the cortex between the medullary rays, furnishing lateral horizontal branches,—the afferent twigs to the Malpighian bodies (*Fig.* 2, AI). Other branches are supplied to the matrix of the kidney and to the capsule, the latter anastomosing with branches of the suprarenal, phrenic, and lumbar arteries.

On leaving the Malpighian body the efferent vessel, which in structure resembles an artery, breaks up into a capillary

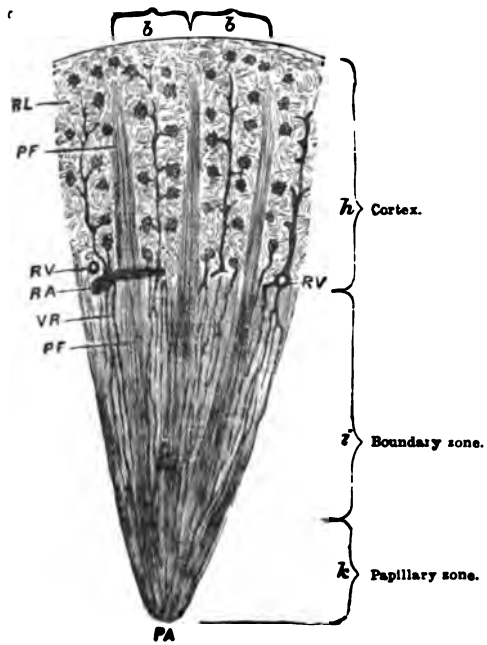

Fig. 2.—Diagram of a pyramid of Malpighi with corresponding cortex (after Landois and Stirling). PF, Pyramids of Ferrein or medullary rays; RA, Branch of renal artery; RV, Branch of renal vein joined by interlobular vein; VR, Vasa recta; PA, Papilla; *b*, *b* embrace the bases of renal lobules.

meshwork surrounding the tubules; from this meshwork venous trunks arise, which terminate in the interlobular veins (*Fig.* 2, VI). The interlobular veins originate just below the capsule as the *venæ stellatæ*. They anastomose freely in the boundary zone, and accompany the arteries to the sinus, where they finally unite to form the *renal vein*.

From the same arches in the boundary zone, formed by the branches of the renal artery after their entrance into the kidney, other vessels arise called the *vasa recta* (*Fig.* 3, VR), which enter the pyramids and pass between the tubules towards the apices.

Some vasa recta are said to arise from efferent vessels which lie near the medulla, or even from the union of the capillaries of the medullary rays (HUSCKE).

In their course through the pyramids they form capillary meshworks around the tubules. From these capillaries venous radicles arise, the *venæ rectæ*, which open into the venous trunks in this region.

The *connective tissue* of the kidney consists mainly of an intertubular stroma, which in the papillæ is broad and fibrous, but in the cortex is more delicate, and is said to be composed almost entirely of branching and anastomosing connective tissue corpuscles (GOODSIR).

Around Bowman's capsules, and continuous with the adventitial coats of the blood vessels, is also a small quantity of white fibrous tissue.

The *ureter* is the duct by which the urine is conveyed to the bladder. It takes origin from the kidney in a number of cup-shaped tubes, called *calices* or infundibula, each of which embraces the apex of a pyramid, or of more than one. The several calices become united to form two or three larger tubes which unite again in the dilated chamber called the pelvis, which is a funnel-shaped expansion of the upper end of the ureter.

Its coats are three in number. An outer *fibrous* coat continuous with the capsule of the kidney and the sheaths of the renal blood vessels.

A *muscular* coat composed of an outer longitudinal and an inner circular layer.

A *mucous* lining consisting of several layers of epithelial cells, round and cylindrical.

Lymphatics of the kidney originate in wide meshed plexuses in the capsule and in large spaces which are more numerous between the convoluted tubules of the cortex, but are also present between the straight tubules.

Large lymphatics provided with valves pass out of the kidney at the hilum, while others emerge through the capsule.

The *nerves* are derived from the renal ganglia and lesser splanchnic nerve. They are gangliated, and contain both

medullated and non-medullated fibres. Their mode of termination is unknown.

Table of weights of the kidneys at different ages (taken from Boyd's tables).

Age.	Sex.	Average weight both kidneys.	Age.	Sex.	Average weight both kidneys.
		oz.			oz.
1 to 2	Male	2·55	30 to 40	Male	11·35
	Female	2·4		Female	10·34
2 to 4	M.	3·33	40 to 50	M.	10·89
	F.	3·14		F.	8·8
4 to 7	M.	4·05	50 to 60	M.	9·1
	F.	4·26		F.	8·55
7 to 14	M.	6·58	60 to 70	M.	8·83
	F.	5·75		F.	8·28
14 to 20	M.	9·34	70 to 80	M.	10·68
	F.	9·09		F.	7·63
20 to 30	M.	11·57	Upwards	M.	8·25
	F.	10·17	of 80	F.	6·86

CHAPTER II.

THE PATHOLOGY OF ALBUMINURIA.

BY Albuminuria we mean the presence in the urine of an albuminous body which is coagulated by heat or precipitated by neutralisation.

Serum albumen is the substance ordinarily found in albuminous urine. It is soluble in water, coagulable by heat at from 73° to 75° C., and precipitated by acids; it is readily soluble in strong nitric acid, and not precipitated by common salt, carbonates of the alkalies or very dilute acids.

Syntonin, or acid albumen, is formed from serum albumen in the presence of a free acid; *alkali-albumen* is a similar modification caused by the presence of a free alkali; these bodies are not coagulated by heat, but are precipitated by neutralisation.

Syntonin may be formed by the careless use of a test tube containing traces of nitric acid.

Alkali-albumen is often present in putrid urine.

Serum globulin is insoluble in distilled water, but dissolves readily in the presence of common salt, and is then coagulable like serum albumen at 73° to 75° C. It may be precipitated from its solutions by carbonic acid gas, or by saturation with common salt or magnesium sulphate. It differs moreover from serum albumen in its more ready diffusibility through animal membranes. It is always present in albuminous urine. In the blood the proportion of serum globulin to serum albumen is as 2 to 3; but in urine, owing to its higher rate of diffusion, this proportion may be reversed. It has been more than once suggested that it is the body present in functional albuminuria or after paroxysmal hæmoglobinuria (GULL, RALFE); but this does not appear to be the case. Out of 16 cases of functional albuminuria examined for this purpose, the albuminous body was pure globulin in only one case, and on a second examination serum albumen was present with it; these results have been confirmed by the more recent observations of Noël Paton and Douglas. It has

been noted to be in excess in cantharides poisoning, in chronic nephritis with waxy degeneration, in the early stage of scarlatinal nephritis, in the albuminuria associated with dyspepsia, in phthisis, etc. Werner found globulin alone present in a case of acute nephritis, and attributed it (following SENATOR) to the destruction of the renal epithelium which contains seven or eight times more globulin than serum albumen. Hermann found globulin to be chiefly present in a case of eclampsia of pregnancy with albuminuria.

Retractile albumen (BOUCHARD) was the name given to albumen which, on boiling, falls down in dense flakes; it was held to be characteristic of Bright's disease. It is worth mentioning in order to note that this has been abundantly proved to be a mistake, this peculiar behaviour being dependent upon the *acidity* of the urine (LÉPINE).

Formerly all albuminates not precipitated by ferro-cyanide were regarded as peptone, until Kühne showed that part of this residue is thrown down by ammonium sulphate, part not. The former is now recognised as albumose, and only the latter called peptone; recent observations have shown that what used to be called *peptone* in the urine is always *albumose* (SCHULTER, SENZ, STOFFREGEN, DEVOTO, THOMSON). *Albumose* is characterized by not being thrown down by heat or by being more easily soluble by heat than in the cold, by being precipitated by ammonium sulphate, and by giving the biuret reaction with solution of copper sulphate. It has been observed to be present in the urine in many acute and chronic diseases, generally in association with serum albuminuria. It must not be assumed that it is necessarily a product of digestion excreted by the kidneys; it is said on good authority (GRÜTZNER) that digestive ferments are present in the urine. According to Mya and Belfanti, trypsin, the normal proteolytic ferment of the urine, is replaced by pepsin in Bright's disease; but either would be capable of effecting the conversion of albumen into albumose,—a process which is probably favoured by elevation of the body temperature in fever, and by the retention of the urine for a certain time in the bladder. Albumose is not coagulable by heat or precipitated by neutralisation; it is thrown down by several of the tests recommended of late years for albumen, *e.g.*, picric acid, metaphosphoric acid, Tanret's test (potassio-mercuric iodide), etc.

Bence Jones's albumen or hemi-albumose, as Salkowski

called it, is a body of doubtful position. According to Salkowski, it remains clear on boiling; it is precipitated on adding acetic acid and common salt solution, but clears up on heating, to be thrown down again on cooling. With pure nitric acid it is precipitated; on heating it dissolves, with the development of an intense yellow colour, and on cooling comes down again. Treated with caustic soda and cautiously with copper sulphate, it gives a purple violet which is lost if excess of copper sulphate is used. With phosphoro-tungstic acid, tannic acid, acetic acid and ferro-cyanide of potassium it is precipitated; but the last reaction does not occur in the presence of ammonia. Heated with a drop of Millon's reagent (acid nitrate of mercury), it gives a deep red colour and precipitate, but this reaction fails when much common salt is present

Bence Jones described the albuminous body in his case as affording the following reactions; he wrote, "The urine that contained it did not give a precipitate immediately by nitric acid, and when heated it did not coagulate, and nitric acid when added to the boiling urine did not give a precipitate. If, after boiling, the urine was cooled, then the precipitate fell, but was immediately redissolved by heat." The difference between this and the reactions given above is that it was not precipitated by nitric acid. Thormählen has described a form of albumen in which the precipitate caused by nitric acid did not re-dissolve on heating, and the solution when cleared by heating, remained clear on cooling. The urine of Joseph B——, a patient in the General Hospital, gave a similar reaction on one occasion.

In the urine of a case of pernicious anæmia I found an albuminous body which presented most of these reactions, but on boiling there was a dense cloud which on adding acetic acid disappeared, while the whole fluid became gelatinised, so that the test tube could be turned upside down. Nitric acid gave a precipitate, but it dissolved on heating without any yellow coloration. Acetic acid and ferro-cyanide of potassium gave no reaction, but this may have been due to the presence of salts of ammonia.

Posner has found hemi-albumose in human semen, as well as in the urine of spermatorrhœa and after pollutions. It has been noticed in many diseases, mollities ossium (BENCE JONES) syphilitic cachexia, diphtheria, cancer of œsophagus, muscular atrophy (SENATOR), petroleum inunction (LASSAR), chronic

nephritis (HOPPE-SEYLER), and therefore has no special clinical significance.

Albuminuria once regarded as diagnostic of Bright's disease has lost this primitive meaning.

The number and variety of the pathological relations under which albumen may appear in the urine compel us to regard it as dependent not only upon inflammation, grave congestions and other coarse organic changes, but upon slight variations in the mechanical conditions of the circulation in the kidney. Excluding accidental admixtures of blood or pus from the bladder or urethra, albuminuria is met with not only in acute and chronic Bright's disease, but in diseases of the heart, lungs, and liver, in peritonitis, pregnancy, abdominal tumours, in most febrile and inflammatory diseases, in many cases of poisoning, in cancer, tubercle and syphilis, in lardaceous disease, in anæmia, debility, dyspepsia, purpura, scurvy, after paroxysmal hæmoglobinuria, in gout, in delirium tremens, in various diseases of the brain and spinal cord, in epilepsy, in certain skin diseases, as well as in apparently healthy persons after bathing, exercise, etc.

All these states are capable of being arranged under the following groups.

1.—*Congestions of the kidney.*

Active or arterial congestion may result from a chill to the skin as in bathing (MAHOMED, JOHNSON); from exposure to cold; from elimination of some irritant through the kidneys such as alcohol, uric acid, phosphorus, lead, cantharides, etc.; from the direct action on the kidneys of a morbid poison derived from the blood, such as the toxins of scarlatina, diphtheria, typhoid, etc., a condition very liable to pass on to acute nephritis; or finally from vaso-motor paralysis after injuries to the spinal cord, and in some other nervous affections.

Passive or venous congestion may result from cardiac, pulmonary or liver disease, peritonitis, pregnancy, abdominal tumours, the hypostatic congestion of prolonged illness, failure of the circulation from enfeebled heart, in fever, in anæmia, in exophthalmic goitre, in fatigue, after violent exertion, *e.g.*, epilepsy.

2.—*Inflammation*, acute or chronic, in many infective diseases, in gout, in chronic lead poisoning, etc.

3.—*New Growths.* Cancer, tubercle or syphilitic deposits in the kidney.

4.—*Degenerations.* Lardaceous degeneration of the renal arterioles.

5.—*Alterations in the composition of the blood*, as in purpura, or scurvy, and after attacks of paroxysmal hæmoglobinuria.

Looked at in this way the difficulties which have beset the discussion of the significance of albuminuria melt away; this result is attained by the absolute surrender of the doctrine that albuminuria signifies Bright's disease, and the acceptance of the view that it is simply the admixture of albumen derived from the blood serum with the urine. It is a fact beyond dispute that albumen may be present in the urine of persons apparently in good health. I do not care to contend that there is not some departure in these cases from the normal mechanism of the renal circulation; but it is certain that neither this lesion nor the loss of albumen gives rise to any derangement of health which impairs the working capacity of the individual or tends to shorten his life; in other words, there are cases of albuminuria which not only do not require medical treatment, but may be safely accepted by life assurance companies. In these cases the urine is normal in every other respect, there are no tube casts, the amount of solid matter excreted is sufficient, and there are no signs of cardiac hypertrophy, of high arterial tension, no retinal changes and no œdema. Leube examined the morning urine of 119 healthy soldiers, of ninety once, of twenty-three twice, and of six three times. Albumen was found six times in the urine of five different soldiers, five times only a trace, once a distinct cloud. The last urine was that of a soldier whose morning urine was examined twice and contained once a distinct cloud, the other time only a trace. The mid-day urine of 119 soldiers was examined, especially that passed after a five hours' march or many hours' parade, in the months of June, July, and August. The five soldiers whose morning urine contained albumen also had albumen in their mid-day urine, three times a trace, three times more distinctly. Moreover, in 148 observations, albumen was found eighteen times in the urine of soldiers whose morning urine was quite free from albumen, in eight distinctly, in ten only a faint trace. The results were that 4·2 per cent. of the soldiers had albumen in their morning urine, and sixteen per cent. had albumen in their mid-day urine. No casts or blood corpuscles were found. All the cases in which albuminuria appeared were carefully examined, and urethral discharges,

as well as signs of Bright's disease, were carefully noted to be absent. The test used was boiling and acetic acid ; but the albuminous body was separated and tested by Millon's reagent, sulphate of copper, ferro-cyanide of potassium, etc.

Grainger Stewart examined the urine of 505 presumably healthy individuals, comprising 205 soldiers of the Seaforth Highlanders, 100 healthy male adults in civil employment, 150 healthy inmates of Craiglockhart Poorhouse (100 adults, over sixty, and 50 children), and 50 children in the Orphan hospital ; of these 166 or 32·8 had albuminuria. Of the 205 soldiers 77, or 37·56 per cent. had albuminuria ; of 100 healthy male adults 10 only ; of 100 inmates of Craiglockhart, about or above sixty years of age, 62 had albuminuria, and of 100 children it was present in 17. Dr. Stirling examined 461 healthy persons of whom 369 were boys, and of these 118 had albuminuria, of whom 77 were boys, giving for adults 44 per cent., for boys 20 per cent. In Leube's cases the albuminuria was found in the mid-day urine four times more frequently than in the morning urine, that is the urine passed immediately on rising. Stirling found the erect posture was the great determining factor in the production of albuminuria in his cases. The same fact is attested by Senator's experience, who found that the urine of himself and three clinical assistants at the Augusta hospital in Berlin repeatedly contained albumen between 11 a.m. and 12.30. Bull has published a case in which the albumen was always absent when the patient was in bed. Marcacci could produce albuminuria in himself by making rotatory movements with his arms for fifteen minutes. It therefore may be accepted that this form of albuminuria in healthy persons depends essentially upon some mechanical condition connected with the erect position and exercise.

Grainger Stewart concludes that albuminuria is more common *in health* as life advances ; but this is doubtful. His elderly people show a high percentage, but there is no evidence that care was taken to eliminate prostatic and vesical catarrh or even latent Bright's disease,—all very common conditions at that age. Other observers have met with functional albuminuria most commonly in young men.

But there are other cases in which some departure from health is present, for example, atonic dyspepsia, with oxaluria or lithuria, anæmia, perhaps not very marked ; or the patient

is an overgrown weakly person, with a tendency to varicose veins in the lower extremities.

In 1876 Moxon described two forms of latent albuminuria. One he called the *albuminuria of adolescence.* It occurs in youths and young men; the patients are languid, perhaps have headache; some slight derangement of the digestive system is often present; there is no evidence of organic disease, and if the urine were not examined the cases would be regarded as debility without any tangible signs of lesion. Albumen is usually found in the urine passed after breakfast, and is nearly surely present in some specimen of the urine collected for a period of forty-eight hours. A few hyaline casts and oxalates are often to be found. In the other form, which he called *remittent albuminuria*, the albumen is present in greater quantity, usually after breakfast, but there is a remission at some period of the day, nearly always in the early morning, so that no albumen is present in the urine passed on rising after a night's rest. These cases have been re-named *cyclical albuminuria* by Dr. Pavy, but it is conceded that the condition depends upon debility and the erect position.

It must be admitted that all our knowledge of these benign forms of albuminuria is recent, and in the face of authorities who maintain that even the smallest trace of albumen in the urine is always pathological, indicating, if not actual disease, a condition of renal stress which sooner or later tends to organic change, it is necessary to state what we know about their subsequent life history. Dr. Moxon mentions that all his cases ended in complete recovery. A medical man has published his own history, showing that from the age of seventeen to thirty-six he had had albuminuria, which was present during the day, but absent when in bed and on first rising; he had enjoyed good general health in spite of hard work of body and mind. Most of my cases have passed out of sight with persisting albuminuria, but some, like the case just related, have lost the symptom and appeared quite well. One of my medical friends at the age of 16 suffered from well-marked remittent albuminuria; he lost it in four or five years, and has never had any trace of kidney disease, though it is now twenty-one years since the albuminuria was first noticed. I see him almost daily, and have often examined his urine. A gentleman was sent to me to be examined for life assurance; he was 46 years of age, and in every respect strong and sound

except that his urine was albuminous; he told me that he was rejected for life assurance for this cause eighteen years before, and that on two subsequent occasions his urine had been examined and found to be in the same state. There was no urethral discharge, and no other evidence of kidney disease. I may also refer to a young gentleman who was sent down from a public school in 1879 with albuminuria, and who was ordered by a London physician to winter in a warm climate as a case of Bright's disease, actually or potentially. This advice was not taken; he has continued to enjoy excellent health, and has always been a very active athlete. If he is going to have Bright's disease he has not yet shown any sign of it. Although I often see him I have not had an opportunity of examining his urine for some years; it formerly contained oxalates, but no casts.

These cases are of practical interest in relation to the question of life assurance. There is great unwillingness to admit that under any circumstances albuminuria can be disregarded. We are told by authority that it is always "a danger signal," and this may be granted readily enough if this is only meant to imply that it calls for the greatest care in the examination of the case, but the time has come to declare that only ignorance of the facts can justify the continued refusal to accept cases where the albuminuria is clearly dependent only on the erect position or on exercise, and the applicant in all other respects satisfies the required standards.

What is the mechanism by which albumen passes into the urinary secretion? Since the time of Bright there have been two rival theories of this process, and of late years a third has been added; these three theories may be called: (1), the Hæmatogenous; (2,) the Parenchymatous; and (3,) the Vascular. There always has been a school which attributed albuminuria not to changes in the kidney but to changes in the blood, and even in Bright's own day he was told that the structural alterations described by him were only the results of the elimination of albumen by the kidneys: this doctrine still survives and finds a persistent defender in Semmola, of Naples. His argument is especially directed to the etiology of Bright's disease, where he contends that the blood contains albuminoids of an abnormal diffusibility, so that they are found in the saliva, sweat and bile,—a fact in which he is supported by Vulpian and others. Tizzoni, however, found that albumen from the urine of a case of Bright's disease did

not cause albuminuria when injected into the circulation of animals. Semmola entirely overlooks all that has been recently observed with regard to albuminuria apart from Bright's disease. Nothing can be farther from the truth than to suppose that the elimination of albumen by the kidney is liable to set up inflammatory action, for we know that it may go on for many years without any such result.

But variations in the diffusibility of the albuminoids of the blood may yet account for albuminuria in certain cases, and there is a great tendency on the part of authorities to accept such a view. Globulin diffuses more rapidly than serum albumen, and it has been stated by Lépine that albumen found in the urine after food diffused more rapidly than that passed fasting. The truth of the doctrine of hæmatogenous albuminuria is by no means bound up with food albuminuria, so that it is perfectly allowable to doubt the occurrence of the latter, while admitting the general probability that changes in the blood account for a certain number of cases of albuminuria ; for example in purpura, scurvy, profound anæmia, after hæmoglobinuria, etc.

With respect to food albuminuria we have Christison's case of the young man whose urine was always albuminous after eating cheese, and the experiments of Brown-Séquard, Barreswil, and others, in which the urine became albuminous on a diet largely composed of eggs. But in the first case the albumen excreted was not shown to be casein, nor in the second to be egg albumen, while more recent experiments have proved that it is not egg albumen * (GRAINGER STEWART), and that it is only when the digestive powers are overtaxed, as by swallowing many raw eggs together, that albuminuria occurs (LAUDER BRUNTON).

Parkes was one of the first to notice that there was an apparent increase of albumen after food. He stated that the albumen was increased after food in two cases of chronic Bright's disease, although it was diminished after food in a case of heart disease. He inclined to the view that the increase after food was due to the passage of imperfectly digested albumen, analogous to that which occurs when albumen is injected into the veins, or to the albumen undergoing some modification in the digestive process, such as its conversion into

* When egg albumen is *injected into the veins*, egg albumen is excreted by the kidneys.

an acid albuminate, by which its diffusibility would be increased.

Parkes's facts do not seem to warrant this conclusion; for, while the albumen was increased after food in the two cases of Bright's disease, it was diminished under similar circumstances in the case of heart disease, so that it is necessary to postulate a peculiar inability to digest albumen in the former cases, which did not exist in the latter. On the other hand, if we regard albuminuria as a result of congestion of the kidney, we can easily understand why, in the cases of chronic Bright's disease, the stimulus to the circulation increased the albuminuria in already inflamed organs, while it diminished it in the case of heart disease, where the transudation was due to passive engorgement of the renal capillaries and veins. But Parkes's views have been adopted by many writers. Pavy supports Parkes by giving a table of the amounts of albumen excreted before and after breakfast in six experiments, all showing a marked increase. Pavy further adopted Parkes's view that this might be due to the increased diffusibility of the albumen, and supported it by showing that in some urines it is highly diffusible; but he did not attempt to prove that the albumen passed after food was more diffusible than that passed before food, or to indicate to what circumstances this increased diffusibility might be due.

Most physiologists deny that unchanged albumen is absorbed into the blood, and the only piece of direct evidence I know to the contrary is the statement of Brücke, that he has found coagulable albumen in the lacteals.

I endeavoured in the first place to determine whether this apparent increase of albumen after food really took place, and the following observations were made on a case of Bright's disease in the Queen's Hospital under the care of Dr. Carter. The patient had been on milk diet previous to this experiment, but on March 10th, 1880, he was put on the following diet:—

Breakfast, 5 a.m., two slices of bread and butter with tea.
Lunch, 10 a.m., two slices of bread and butter with one pint of milk.
Dinner, 1 p.m., four ounces of cooked meat, eight ounces of potatoes, bread and water.
Tea, 6 p.m., the same as breakfast.
Supper, 7 p.m., half-pint of milk.
He took walking exercise twice daily for half an hour at 12.20 and 2.30

Date.	Period.	Quantity of Urine.	Albumen in 40 ccms.	Total Albumen.
March 10	7 P.M. to 5 A.M.	1620 cc.	·008 grms.	·1296 grm.
„	5 A.M. to 1 P.M.	150 cc.	·016 „	·06 „
„	1 P.M. to 5 P.M.	180 cc.	·01 „	·045 „
„	5 P.M. to 7 P.M.	120 cc.	·008 „	·024 „
„ 12	7 P.M. to 5 A.M.	870 cc.	·0069 „	·1479 „
„	5 A.M. to 1 P.M.	180 cc.	·017 „	·0756 „
„	1 P.M. to 5 P.M.	180 cc.	·0141 „	·0630 „
„	5 P.M. to 7 P.M.	150 cc.	·009 „	·0330 „
„ 13	7 P.M. to 5 A.M.	1410 cc.	·0155 „	·5358 „
„	5 A.M. to 1 P.M.	180 cc.	·020 „	·090 „
„	1 P.M. to 5 P.M.	180 cc.	·0166 „	·0738 „
„	5 P.M. to 7 P.M.	120 cc.	·015 „	·0444 „

On each day, the relatively greatest quantity of albumen was excreted between breakfast and dinner. The quantity each day fell as the day advanced, in spite of the meat eaten at dinner, and the exercise taken in the afternoon. The total quantity of albumen excreted rose steadily under the influence of meat diet, being three times greater on the fourth day than on the first.

One bottle containing the urine of part of March 11th got broken, so that day's record was incomplete. The analyses were performed by Dr. MacMunn.

This observation is opposed to the doctrine of Parkes that unassimilated albumen is excreted by the kidneys. But it has been suggested that after food there may be a more rapidly diffusible albumen present in the blood. That there should be such differences is quite probable, as Graham long ago pointed out that an acid solution of albumen diffuses readily, while an alkaline solution scarcely diffuses at all; so that differences in the alkalinity of the blood serum may determine variations in the amount of albumen excreted. Pavy showed, using pericardium as a membrane, that egg albumen diffuses more readily than serum albumen, and Lépine has filled up the gap left by Pavy by observing that albumen in the urine after food diffused more rapidly than that passed fasting. The following experiments appear to show that the results may depend upon variations in acidity, etc., and not upon any primary difference in the albumen itself.

The septum used was vegetable parchment; and the time allowed was twenty-four hours in each case.

The following experiments were made on the urine of the same case :—

Experiment I.—*Before breakfast:* In bed. Urine faintly acid ; one-third of a column of albumen ; no albumen in diffusate.—*After breakfast:* In bed. Urine acid ; four-fifths of a column of albumen ; a trace of albumen in diffusate.

Experiment II.—*Before breakfast:* In bed. Urine neutral ; a trace of albumen in diffusate.—*After breakfast:* In bed. Urine acid ; a trace in diffusate.

Experiment III.—*Before breakfast:* In bed. Urine faintly acid ; one third of a column of albumen ; a faint trace in diffusate.—*After breakfast:* In bed. Urine acid ; two-thirds of a column ; a trace in diffusate.

Experiment IV.—*Before breakfast:* In bed. Urine faintly acid ; one-third of a column of albumen ; a trace in diffusate.—*After breakfast:* In bed. Urine acid ; two-thirds of a column of albumen ; a trace in diffusate.

Experiment V.—*Before dinner:* Up. Urine neutral ; a distinct cloud in diffusate.—*After dinner:* Up. Urine acid ; a distinct cloud in diffusate, but less than before dinner.

Experiment VI.—*Before dinner:* Up. Urine acid ; half a column of albumen ; a cloud in diffusate.—*After dinner:* Up. Urine strongly acid ; a whole column of albumen ; a dense cloud in diffusate.

Experiment VII.—*Before dinner:* Up. Urine acid ; half a column of albumen ; a faint trace in diffusate.—*After dinner:* Up. Urine faintly acid ; one-third of a column of albumen ; a faint trace in diffusate.

As a rule, the albumen appeared to diffuse in proportion to the acidity of the urine. The diffusate bore no relation to the quantity of albumen present in the urine.

While it is fully admitted that more carefully conducted experiments might determine differences in diffusibility due as suggested to alterations in the salts of the blood or the alkalinity of the blood serum, there is no evidence that undigested albumen is ever excreted by the kidneys ; and in this shape the doctrine of food albuminuria must be abandoned.

The parenchymatous theory ascribes the albuminuria to the destruction of the epithelial lining of the renal tubules, but there are several hypotheses which are strongly opposed to one another. One of the most interesting, that of Von Wittich, adopted by Ludwig, and lately revived in Glasgow, is that albumen is physiologically transuded through the Malpighian

tufts, but reabsorbed by the epithelium of the tubules. When the parenchyma is diseased this reabsorption is more or less hindered and albuminuria results. This theory, attractive as it is, is disposed of by the experiments of Posner and Ribbert, who proved by boiling freshly excised kidneys and hardening them in alcohol that there is no albumen present in the capsular space around the Malpighian tuft in healthy kidneys, though it can be easily demonstrated in albuminuric kidneys even when the epithelium is intact.

Another form of the parenchymatous hypothesis is that when the parenchyma has been shed from the tubules the basement membrane permits the transudation of albumen. This theory has never been disproved ; and it is in its favour that kidneys prepared by the boiling and alcohol method showed albumen in the straight tubes ten minutes after ligature of the renal vein.

A third suggestion made by Senator is that the destruction of the renal epithelium itself furnishes a sensible amount of albumen. In the early stage of nephritis the epithelial cells shed their protoplasmic contents into the lumina of the tubules. This would only apply to cases of irritative or inflammatory albuminuria.

Lastly, there is the vascular theory. The ordinary seat of the transudation of albumen has been shown by Posner to be the Malpighian tufts ; as was suggested by an experiment of Nussbaum's. In frogs the veins of the posterior extremities divide in the pelvis into two branches, one of which passes to the kidney like a portal vein, while the other joins its fellow of the opposite side to form the vena abdominalis anterior. The blood in the other branch passes through the kidneys and the liver into the vena cava inferior to reach the right side of the heart. The renal glomeruli receive their blood from the renal arteries, and the vasa efferentia pass into the same capillary network as that supplied by the renal portal veins, so that by tying the renal arteries in frogs the renal circulation is not brought to a stand-still as it is in mammalia. Taking advantage of this anatomical fact, Nussbaum tied the renal arteries, and then injected a five per cent. solution of egg albumen or a ten per cent. solution of peptone into the anterior abdominal vein without causing albuminuria, although when the renal arteries were not tied a smaller quantity sufficed to produce albuminuria. It is therefore proved that in frogs an albuminuric dyscrasia causes transudation of albumen only

through the glomeruli, and it is probable that this is also true in man ; taken together with Posner's observations we may regard the point as practically determined in that sense.

The question is, What causes the transudation? Is there a physical change in the membrane, or is there some alteration in the blood pressure or the rapidity of the blood current? These questions have given rise to much discussion. Thoma showed that in contracting kidney the walls of the glomeruli are actually abnormally permeable, permitting the passage, not only of thin fluids and colloids, but of small solids such as crystals of cinnabar, and this, too, in parts of the kidney presenting no recognisable structural alteration ; but observations are wanting to enable us to extend this to other conditions under which albuminuria occurs. We know that very slight alterations in the coats of the vessels, such as may be induced by temporarily clamping or ligaturing the renal artery, give rise to albuminuria, and this may follow simple persistent blocking of the ureter. The action of certain poisons, for example, carbolic acid, has been proved by boiling, and hardening the kidneys in alcohol, to cause albumen to transude through the glomerular wall without any visible structural alteration taking place (RIBBERT).

It must therefore be allowed that such changes may account for certain forms of albuminuria. But there are other important factors in this vascular theory, especially the pressure and rapidity of the circulation. Since Robinson experimented by tying the abdominal aorta below the origin of the renal arteries, the influence of increased blood pressure in determining albuminuria has been generally recognised; but of late years it has been called in question. It is fully admitted that the amount of urinary secretion varies directly with the pressure ; but Runeberg has contended that the amount of albumen varies inversely. Lépine supports this in the following table :—

Pressure.	Albumen.
100 c.c.	1·3, 1·077, 0·66
40 c.c.	0·95, 1·5
100 c.c.	1, 0·7, 0·6
40 c.c.	0·8, 1·3, 1·4, 1·5

Senator accepts this view, and holds that the higher the pressure the more water but the less albumen. Bamberger also believes the albumen to be diminished as the pressure rises. Löbisch and Rokitansky caused albuminuria in healthy

persons by lowering the blood pressure with pilocarpine. There can be no doubt that increased venous pressure leads to albuminuria as is seen clinically in cases of heart, lung, and liver disease, pregnancy, abdominal tumour, and probably too in many cases of debility, anæmia, and in the hypostatic congestion of fevers, pneumonia, etc. In ligature of the renal vein albuminuria occurs rapidly, and has been proved by Senator to take place by direct transudation into the tubules, probably from the lymphatics. Charcot and Bamberger attach much importance to the influence of slowing the current, which is shown by physical experiment to favour the filtration of albumen.

Ischæmia of the kidney, by experimental narrowing of the renal artery, leads to albuminuria, probably by slowing the current and reducing the pressure. Claude Bernard's puncture and experimental lesions of the spinal cord give rise to albuminuria by vaso-motor paralysis, the kidneys being deeply congested (SCHIFF). Many of the cases which have been regarded as neurotic albuminuria are susceptible of a more simple explanation, as has been already suggested for epilepsy and tetanus; and it will be admitted that other conditions are present in exophthalmic goitre, besides the nervous disturbance, sufficient to account for albuminuria, though this may be due in part to altered vascular innervation.

We may usefully summarise the teachings of this lecture in the following conclusions :—

1.—Albuminuria is defined as the presence in the urine of serum albumen, or serum globulin, or their modifications, syntonin and alkali albumen.

2.—Albuminuria may be present in healthy persons and persist for long periods without causing any derangement of the general health, or of the structure of the kidneys.

3.—Albuminuria *per se* should not be regarded as an insuperable objection to life insurance.

4.—Albuminuria may occur in dyspeptic people, and in weakly over-grown persons, without being an indication of actual or potential renal disease.

5.—Albuminuria may depend upon many causes, grouped under three headings: (1), Hæmatogenous: due to alterations in the diffusibility of the blood albuminoids, owing to changes in the salts of the blood or the alkalinity of the blood serum; but albuminuria is never due, as has been asserted, to the excretion of undigested or partly digested albumen taken as

food. (2), Parenchymatous: inflammatory changes in the epithelium give rise in the first instance to an albuminous exudate which must be present in the urine, and secondly by destroying the cell layer and altering the basement membrane, allow direct transudation from the lymphatic vessels into the tubules. (3), Vascular: the walls of the glomeruli probably undergo alterations of their permeability from the effects of poisons, inflammation and vaso-motor paralysis, while lowering of the blood pressure and slowing of the blood current favour filtration of albumen through them. In venous obstruction there is œdema of the whole organ and transudation of albuminous fluid direct from the lymphatic spaces into the tubules; in inflammation and vaso-motor paralysis a similar œdema is likely to occur with identical results.

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CHAPTER III.

THE PATHOLOGY OF DROPSY.

DROPSY is certainly the most striking symptom of Bright's disease, and the one that commonly first attracts the patient's attention, but the proportion varies in the different forms of Bright's disease. It is usually present in acute nephritis, but it may be very slight or altogether absent. Thus it is commonly absent in cases of acute nephritis supervening in the course of pneumonia, diphtheria, typhoid fever, etc., though the state of the urine proves incontestably that acute nephritis exists. In subacute nephritis and in large white kidney, dropsy is very common, being absent in only eight or ten per cent. In the contracting form it is much less common; in the earlier stages it is generally absent, but later on it is more frequent. Thus, out of a hundred cases seen in the out-patient department, I found dropsy present in ten per cent. only, while in the bodies of persons who had died with contracting kidney, I found the proportion as high as twenty-five per cent. This variation is fully explained by the cause of the dropsy, which in contracting kidney must for the most part be attributed to heart failure. So long as the hypertrophied heart can do its work all goes on fairly well; but when this organ at last breaks down, dropsy appears along with other signs of collapse of the whole system. Like ordinary cardiac dropsy, it is first seen in the legs and ankles, increasing after rising or getting about, and must be regarded as of grave prognosis, indicating failure of the heart to maintain the struggle any longer.

The fluid in renal dropsy varies in different situations, being poorer in albumen and solids in the subcutaneous tissue than in the serous sacs. The following table taken from Bartels gives the composition in the various seats of dropsy.

	Sp. g.	Water.	Solids.	Inorganic Salts.	Albumen.
Blood Serum.....	1015·58	957·656	41·402		30·39
Pericardial fluid	1009·69	978·622	21·38	15·58	?
Peritoneal „	1009·63	984·31	15·69	14·48	2·55
Subcutaneous „	1007·65	988·30	11·70	11·69	

Schmidt gives the following figures :—

Subcutaneous tissue, 0·36% albumen ; Meninges, 0·6 to 0·8 % ; Peritoneum, 1·13 % ; and Pleura, 2·85 %.

Urea has been found in it by many observers, and Bartels quotes the following figures from Edlefsen :—

Subcutaneous tissue, 0·359 % ; Peritoneum, 0·28 to 0·30 %; Pericardium, 1 %.

What is dropsy? Dropsy consists in an accumulation of watery fluid in the lymph spaces of the subcutaneous cellular tissue and in the serous cavities of the body. This fluid or lymph is derived from the capillaries, and under normal circumstances is poured out into these spaces, but taken up again by the venous and lymphatic radicles as fast as it is poured out.

For the production of dropsy, the equilibrium of this arrangement must be upset by either (*a*) an increase in the outflow of fluid, or (*b*) a failure on the part of the veins and lymphatics to take up the effused fluid.

An increase in the outflow of lymph from the capillaries is caused experimentally by section of the vaso-motor nerves, and occurs in disease when their function is paralysed ; it may also be due theoretically to increased permeability of the vascular walls, and to changes in the blood serum. We shall afterwards see what share to assign to each of these factors.

The principal source of power in pumping these lymph spaces dry is the heart ; it is assisted by the aspiratory action of the thorax in respiration, and the contractions of the muscles in the limbs. When the heart fails to maintain a negative pressure in the veins œdema sets in. Localised venous obstruction acts with less certainty in the same way, as the lymphatics which open into the venous circulation beyond the obstruction may carry on the work ; if, however, their task is added to by cutting the vaso-motor nerves, and so leading to a greater influx of blood to the capillaries and increase in the outflow of lymph, dropsy sets in. Section of the nerves probably has more than this simple effect, but it need not concern us at present. There are no difficulties in the way of understanding dropsy due to heart failure ; it is a break down in the central pumping apparatus, and need not detain us longer.

The dropsy of acute nephritis presents problems of greater difficulty. In most cases there can be no question of heart failure, and its explanation must be sought for in the factors that determine an excessive outpouring of lymph from the

blood vessels. In acute Bright's disease the urinary secretion is very scanty, and as patients continue to swallow fluids the total quantity of blood must increase absolutely in volume while suffering a relative diminution of its solids; that is to say, the water is absolutely increased and the solids relatively decreased, inducing a state of hydræmic plethora.

A watery condition of the blood has long been regarded as a cause of dropsy, some authors seeing in it a predisposing factor, others ascribing to it still greater importance. Brücke's experiment of cutting one sciatic nerve of a frog and putting the animal on a piece of moist blotting paper in a large glass vessel, showed that after some weeks œdema occurred in the palsied limb, which disappeared on food being administered, reappeared in inanition, and disappeared again when nutrition was restored. But there is considerable difficulty in ascertaining what are the circumstances under which hydræmia will produce dropsy, for authorities certainly differ as they are wont to do.

One of our earliest experimenters, Hales, succeeded in producing "both the ascites and the anasarca" in a dog by pouring water into the jugular vein, but when we read the description it appears that the dog died during the progress of the experiment, and we are not told whether these phenomena preceded death or not; this is an important point, as the retentive power of the vascular walls alters altogether after death. Magendie in his "Leçons sur les Phénomènes Physiques de la Vie" alludes to this matter in several lectures; he certainly tells us that he succeeded in producing general dropsy by defibrinating the blood of a dog, and in another experiment he produced analogous results by pouring water into the veins, as Hales had done. But he performed a much more remarkable experiment by introducing no less than ten litres of water into the veins of a patient suffering from hydrophobia; he had observed the wonderful calmative influence which similar injections had upon ferocious dogs, and he hoped by this means to combat this fatal disease. His patient lived several days, and died presenting the phenomena of several "pseudarthroses" or dropsical swellings of joints. We are not told that œdema was absent, but from the relation the story bears to the main point of the lecture, we may feel justified in concluding that had there been any anasarca, the lecturer would not have failed to mention it.

Niemeyer states—I know not on whose authority—that "if we abstract blood from an animal and inject a corresponding quantity of water into its veins in its stead, the animal does not become dropsical"; on the other hand, Jaccoud says "the artificial dyscrasia created by the injection of water is rapidly and constantly followed by temporary dropsy." Wagner quotes Donders, Kierulf and Hermann in proof that dropsy may be caused by the injection of abundance of water into the circulation; but to this is opposed the experiment of Cohnheim, which showed that a solution of salt might be passed under low pressure through a limited vascular area, such as the ear of a rabbit, without causing œdema. It is obvious that all these experiments do not fulfil the conditions necessary to throw light upon the influence which hydræmia may have in producing dropsy in certain diseases. Injections of pure water destroy the blood corpuscles, and paralyse the heart, as well as, in all probability, the walls of the blood-vessels; while the pressure employed by some of the observers was probably greater than the normal blood pressure of the animal.

Bartels ranged himself very unreservedly on the side of those who regard the hydræmia of Bright's disease as the efficient cause of the dropsy, but he thought there had been much confusion in the minds of many physicians who supported this view, as to the cause of the watery state of the blood. He admitted that in renal diseases a large quantity of serum albumen is lost by the blood, and he believed that this must render the blood serum more watery; still, he was of opinion that this is neither the sole nor the essential cause of the hydræmia, for renal disease may lead to most extensive dropsy before any quantity of albumen worth mentioning has been eliminated; and he regarded the occurrence of dropsy as dependent less upon the loss of albumen than upon the diminution of the amount of water secreted by the kidney. Even in cardiac disease, he said, we see the influence of the quantity of the renal secretion on the presence of œdema, and he denied that the malnutrition existing has anything considerable to do with the matter. On the other hand, in renal disease a considerable daily loss of albumen may take place without any dropsy resulting if only the quantity of water passed is sufficiently copious, while dropsy may ensue during an insignificant loss of albumen directly the daily urinary secretion falls below a certain minimum quantity.

He quoted the observations of Rehder, who, with the view of establishing the proportion borne by the quantity of water taken in drink and food towards that which afterwards appears in the urine, instituted a series of experiments upon healthy persons living under identical external conditions and then compared the results with a series of analogous observations made on dropsical subjects.

Rehder subjected five healthy persons to experiment, and the average of the daily results, extending over thirty-two days, was, that of every hundred parts of fluid ingested, 76·4 parts were excreted in the urine; the lowest mean in one individual was 68 per cent., the highest 88 per cent. Very contrary results were obtained by the observations on persons suffering from cardiac and renal dropsy. A man aged fifty, with cardiac disease, excreted quantities of water varying from 29·7 to 49·2 per cent.; a youth with chronic parenchymatous nephritis excreted 18·6 to 33·5 per cent. only; in a woman with the same disease the excreted water averaged 16 per cent., and never exceeded 24·4 per cent.; a man with the same gave an average of 28 per cent. In another case the exact correspondence between the increase and subsidence of the anasarca and the diminution and increase of the urinary secretion was perfectly established.

Bartels held that these experiments show that the dropsy of renal disease is due to the relative insufficiency of the kidneys to eliminate water; but some time must elapse before anasarca occurs; in one case, in which stoppage of both ureters was present, one hundred and twenty-two hours elapsed without a trace of œdema showing itself, but this patient vomited large quantities of liquid.

The cases given by Trousseau of two patients suffering from general anasarca due simply to retention of urine, and whose symptoms were completely relieved by emptying the bladder, are, if any be needed, additional clinical illustrations of the dependence of dropsy on a free exit of water by the kidneys.

Cohnheim and Lichtheim directly oppose Bartels' view, and they have endeavoured to show that hydræmia *per se* cannot produce subcutaneous œdema. Their experiments were made by injecting, with a syringe or under very low constant pressure, large quantities of a blood-warm 0·6 per cent. solution of common salt into the circulation of dogs, rabbits, and other animals; rabbits were used without any preparation, but dogs and the larger animals were soothed with morphia or curarised.

As a preliminary proceeding they endeavoured to gain some idea of the quantity of fluid which might be injected without killing the animal, and they found that dogs could stand much more than rabbits; the latter generally could support an injection of 46 per cent. of their body weight before they died, but dogs withstood a much greater quantity, especially if the abdominal cavity were opened, 92 per cent. of his body weight being introduced into one dog before he died. In one case the dog died of acute œdema of the lung, but they were unable to account for this exceptional occurrence; in general the animals died with symptoms of deoxygenation of the blood, paralysis of the heart, and in some cases convulsions.

In none of these experiments—and they were very numerous—was any subcutaneous œdema or anasarca produced; even after the largest injections the subcutaneous tissue was quite free from water, and as this is the earliest and principal seat of the so-called hydræmic œdema, it appeared from these observations that hydræmic plethora had nothing to do with hydræmic œdema. The following figures show the amount of hydræmia they produced:—They found the normal dried residue of a dog's blood to be about 20 per cent., the highest being 24·09 per cent.; Andral and Gavarret found the dried residue of the blood of a case of kidney disease to be 13·23 per cent.; in their experiments the percentage fell from 22·05 per cent. to 11·64 in one case; in another from 20·76 to 11·33; in a third, with the abdomen open, from 22·16 to 8·29 per cent. A still greater degree of hydræmia was produced by ligaturing the whole portal circulation; for example, in one case in which the cœliac, superior and inferior mesenteric arteries and the portal vein were ligatured, the percentage fell from 24·09 to 4·87.

Many authors have considered the hydræmia of renal dropsy as it affects not the entire solids of the blood but those of the blood serum. Christison found these to be 6·1 per cent., and Frerichs, in three cases of commencing nephritis, found them 9·19 per cent. In one of their cases, after injecting 64 per cent. of the body weight of common salt solution the serum residue was only 2 per cent., so that there can be no doubt that the thinning of the blood produced in these experiments not only equalled but exceeded that which occurs in disease, and the absence of anasarca cannot be thus explained.

In the next place they proceeded to enquire what influence hydræmic plethora had upon the pressure and rapidity of the blood current; this is of especial interest with reference to the views of Traube, who regarded the increased arterial tension and the hypertrophy of the left ventricle as the result of the diminished secretion of water, and the resulting hydræmic plethora. They could not succeed in raising the pressure above the normal except momentarily, and they found important increase of pressure to occur only when it had previously been below normal. The shape of the curve of the blood-pressure underwent remarkable changes during the experiments; at first the respiratory wave disappeared and only the pulse wave remained, but got much larger; after a time the curve resumed its original outline. A similar negative result followed experiments on the venous pressure; a slight increase was produced temporarily, and was accompanied by a venous pulse proved to originate by back-stroke from the heart. The blood current was *quickened;* this was directly observed in the mesentery and tongue of frogs, but it did not last long. They observed the same in the mesentery of dogs and rabbits, and also by counting the blood drops from the vein of the anterior extremity of a dog; although this method cannot be exact, the increase was too enormous to leave any doubt.

The most obvious appearance was transudation of water from the blood, not only through the glandular organs, but into their tissues themselves. The first point seems to indicate that all glandular organs secrete a very large quantity of water. The animals passed a very large quantity of pale limpid urine, which in some rare cases contained a small quantity of albumen, and more frequently but not constantly, sugar, which had been previously recorded by Bock and Hoffmann. The saliva and the secretions of the glands of the mouth were increased enormously, also the secretions of the gastric and intestinal glands; the bile was richly secreted, but the pancreatic fluid was not increased. The secretion of the conjunctiva, lachrymal glands and mucous membrane of the nose was greater than normal, and the perspiration in two experiments on a goat and on a horse was very profuse.

In order to estimate the part played by the absorbents, a cannula was placed in the thoracic duct and an enormous acceleration of the lymph stream was demonstrated, but it is remarkable that when the cannula was placed in the lymphatic

trunk of an extremity no acceleration of the lymph stream could be produced; between these two extremes the lymphatics of the neck showed a definite increase, but not nearly equal to what was observed in the thoracic duct. These differences correspond to the differences produced by hydræmic plethora in different parts; for although no œdema of the subcutaneous connective tissue was ever observed, there was a special localisation of the dropsy which the authors believed to be characteristic of the dropsy of hydræmic plethora.

The bodies of the animals swelled very much, and the peritoneal cavity was always full of fluid, as were the intestines, while their mucous and submucous coats were œdematous; the coats of the stomach presented a still higher grade of œdematous swelling. The lymphatics and chyle ducts of the mesentery were distended and the mesenteric lymph glands were swollen and œdematous. The pancreas presented the most extreme degree of dropsical distension; the kidneys were both enlarged, pale, and extremely moist on section; the liver was distended, of doughy consistence, and on section discharged a large quantity of thin watery blood; the gall bladder was very œdematous, its wall being more than a millimetre thick. The vesiculæ seminales and the retroperitoneal tissue were also œdematous. The spleen was somewhat swollen and tight to the feel, but frequently scarcely at all enlarged. The thoracic cavities and viscera presented a striking contrast; neither pericardium nor pleural cavities contained a drop of fluid; the lungs (except in one case, in which they were œdematous) were quite dry, or at most there was only slight œdema of the connective tissue bands radiating from the hilus. The sub-maxillary, salivary and lymphatic glands were swollen, as were the sublingual glands and the lymphatic glands of the neck. The conjunctivæ and lachrymal glands were œdematous. All other organs, such as those of the central nervous system, were free from œdema.

These results were uniformly the same in all their numerous experiments. In order to exclude the possible objection that by injection into the jugular vein, the fluid was driven directly into the inferior cava and the veins of the liver so as to cause a special obstruction of the portal circulation, they injected fluid into the femoral vein or into an artery, and got the same results.

They varied their experiments by using other fluids;

distilled water killed the animals too soon by destroying the blood corpuscles, but solutions of sugar, various salts, albumen and blood serum gave the same results as the solution of common salt. They also used defibrinated dog's blood in a few cases, and, except that the resulting œdema was much less, often somewhat sanguineous, and complicated by punctiform hæmorrhages, the results were the same as before.

Again, they bled dogs and injected an equal quantity of salt solution, without causing anything at all except slight œdema around the operation wound. But, as it might be questioned whether the skin of dogs and rabbits is analogous to that of man, more especially as the important sweat function of the latter is absent in these animals, they performed experiments on a horse and a goat. Both animals died of œdema of the lung; before death there was copious perspiration, but no subcutaneous œdema.

The following circumstance appeared to throw some light upon the occurrence of œdema. In fixing their dogs for experiment they used to place an iron ring between their toes and fasten this to their noses by a loop; they noticed that the snouts of the animals became œdematous; they repeated the experiments on animals with wounds, and found that œdema occurred around the wound. Painting with iodine always produced slight subcutaneous œdema, but animals so treated showed marked œdema after hydræmic plethora was induced. They produced the most superficial dermatitis by shaving animals and exposing them to the sun's rays for an hour or two, and the slight œdema resulting was greatly increased by hydræmic plethora. Tying the femoral vein of a dog produces no œdema of the corresponding foot, but this occurred frequently when the blood was thinned.

They argue from these facts that some change in the state of the vessels is the necessary factor for the occurrence of œdema in hydræmia; and while they admit that it is not easy to explain renal dropsy by any demonstrated changes in the cutaneous vessels, the combination in scarlatina is very noteworthy. In this disease along with the skin affection there is often slight œdema, which becomes very pronounced on the supervention of suppression of urinary secretion by renal disease and the consequent hydræmic plethora; occasionally the changes in the skin vessels are sufficiently great to cause œdema, apart from renal mischief, forming the long recognised *hydrops scarlatinosus* without albuminuria.

The frequent absence of dropsy in the acute nephritis of pneumonia, diphtheria and other non-eruptive infective diseases already alluded to, supports this explanation.

In the hydræmic dropsies of cachectic diseases they suppose that the prolonged hydræmia injures the walls of the vessels.

Although it is competent to deny the parallelism of these experimental conditions with those of disease, we must admit that they corroborate the previously alluded to experiment of Cohnheim, that watery solutions of common salt at the temperature of the body do not readily pass through the walls of the subcutaneous vessels; and there seems reason to doubt whether, volume and pressure remaining the same, simple hydræmia can by itself induce œdema. We know that inanition rarely produces dropsy in the human subject; patients suffering from malignant stricture of the œsophagus often present the most extreme degree of emaciation without any or with the slightest possible dropsical swelling. Virchow noticed no dropsy in the famine in the provinces of Upper Silesia and Spessart; individuals who suffer from most profound anæmia from hæmorrhages rarely show corresponding œdema.

Many cases of total suppression of urine from calculous obstruction have been observed without œdema, but there is frequently constant vomiting which would tend to prevent an increase in the volume of fluid in the circulation.

In hysterical oliguria there may be an extreme reduction of the urinary secretion without œdema or vomiting. In a case seen by me with Mr. Lawson Tait in September, 1885, a lady passed only 16 ounces of urine in a week, without dropsy, vomiting, or uræmic symptoms. She was under close observation in Mr. Tait's private hospital, so that there can be no room for doubt as to the facts.

We are therefore driven to look to a third factor, increased permeability of the vessels, to fully explain the dropsy of acute nephritis. What the exact nature of the physical change is, remains obscure. Cohnheim, perceiving its analogy with what occurs in inflammation, calls it an "inflammatory" change; he believes that it may be brought about when hydræmia has persisted for a long time. It is probably influenced by the innervation of the blood vessels. Landois says it occurs when the blood contains dissolved hæmoglobin or too little oxygen or albumen. Lauder Brunton has found that the permeability of the vessels after death is increased

by the presence of acids in the blood, and suggests that acids or substances acting in the same way may accumulate in the blood in Bright's disease. He quotes from an inauguration thesis by Feitelberg, who shows that a number of poisons, among them arsenic, have the power of increasing the acidity of the blood; and he recalls the œdematous condition of the eyelids induced by arsenic as an illustration to the point. This is all that is at present known on the subject.

Summary.—1. Dropsy is an accumulation of lymph or watery fluid in the lymph spaces of the body as a consequence of—(*a*) defective pumping arrangements, by which the fluid is allowed to accumulate; (*b*) changes in the blood and capillaries by which the outflow of fluid is increased.

2. Dropsy is generally present in acute and sub-acute nephritis, and in about 90 per cent. of cases of large white kidney; but in uncomplicated contracting kidney it is absent in at least 90 per cent. of those able to get about. In the later stages of contracting kidney it is more frequent, being present in 25 per cent.

3. In uncomplicated contracting kidney dropsy is due to heart failure; but in acute nephritis and its sequelæ it is due to more obscure causes in which a watery state of the blood is accompanied by increased permeability of the capillaries, caused possibly by the presence of an acid or other toxic substance in the blood.

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CHAPTER IV.

PATHOLOGICAL RELATIONS OF TUBE CASTS.

SINCE it has been shown beyond dispute that albuminuria may be present not only in acute diseases, but in various chronic maladies, apart from renal inflammation, and even under certain circumstances in healthy men, it has lost its former significance as evidence of Bright's disease.

Moreover, we know that Bright's disease may be present, and progress to its termination (BARTELS) without the occurrence of albuminuria; so that we stand greatly in need of some more trustworthy sign.

If in recent years the discovery of tube casts in the urine of patients suffering from jaundice, diabetes and secondary congestions of the kidneys, or even in more transitory conditions, as in the urine of the famous pedestrian Weston, during his prolonged walk, may have appeared to throw a little doubt on their diagnostic value, it is certain that they afford us the best and clearest indications of the changes that are taking place in the renal epithelium,—changes which rightly interpreted afford the safest grounds for diagnosis and prognosis.

Varieties of Casts. Casts of the renal tubules are of three kinds: (1,) Blood Casts; (2,) Epithelial Casts; (3,) Hyaline Casts.

There are also mixed varieties, blood or epithelium adhering to or forming part of a hyaline cast; and the term "granular" is frequently used to describe either epithelial or hyaline casts, which have become opaque and granular from infiltration with fat granules or micro-organisms.

Blood Casts. Casts composed of blood clot, *i.e.*, blood corpuscles matted together with fibrin (*Fig.* 4, *a*) indicate as may be supposed, the entrance of blood into the tubules of the kidney. The source of the hæmorrhage is for the most part the capillary tufts of the Malpighian bodies. The blood in its passage down the tubes becomes coagulated, and passes into the urine in the shape of cylindrical casts of the tubules. The presence of such casts affords important evidence in hæma-

turia, proving that the blood comes from the glandular substance of the kidney, and not from the renal pelvis as in calculus of the kidney, or from any lower part of the urinary tract. These casts are seen in the early stages of acute nephritis, so long as hæmaturia persists, or when it occurs in any form of Bright's disease, as well as in hæmorrhage from congestion. They must therefore be regarded as evidences only of rupture of blood vessels in the glandular part of the kidney, and not as signs of any stage or form of Bright's disease.

Epithelial Casts. There are two main types under which the renal epithelium appears in the urine under the form of

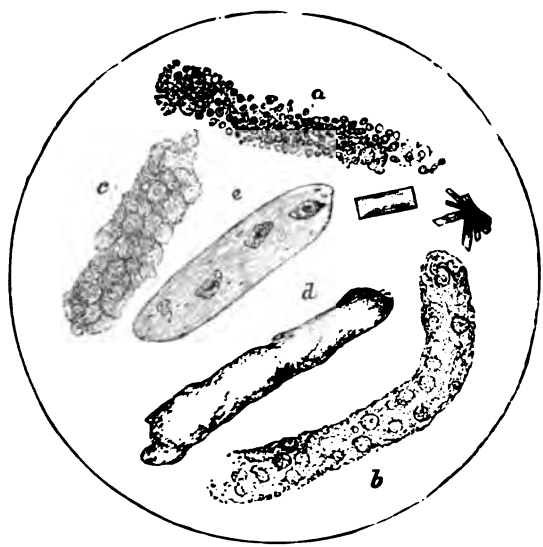

Fig. 4. Varieties of tube casts: *a*, Blood cast; *b*, Epithelial cast composed of small round cells; *c*, Epithelial cast formed of desquamated and fatty epithelium; *d*, Granular hyaline cast; *e*, Hyalo-epithelial cast.

casts of the tubules of the kidney. In one the cast is made up of distinct small round granular cells, like leucocytes, but of smaller size, and which are, as their appearance suggests, proliferated renal epithelium (*Fig.* 4, *b*).

These are met with in acute and sub-acute nephritis, and always indicate an active degree of inflammation, with proliferation of the renal epithelium.

In the second type the cast is composed of a mass of epithelial cells, crowded together so as to obscure their

individual outlines, and more or less opaque from fatty degeneration (*Fig.* 4, *c*).

These are formed by the desquamation of the epithelium, which is pushed off the basement membrane by the inflammatory exudation from the venous plexuses surrounding the tubule; they are usually of large diameter, being moulded in tubes denuded of epithelium, and they witness to severe diffuse inflammation of the kidney. They are met with in cases of recent inflammation in healthy kidneys, in sub-acute nephritis, and in the acute and sub-acute attacks which so frequently supervene in the course of the contracting kidney.

Hyaline or Colloid Casts. These are by far the most common casts; they are met with in all forms of Bright's disease, in venous congestion, and in many conditions where the kidney is undergoing slight or temporary irritation. They occur in jaundice, diabetes, heart disease, and pregnancy; they were found in the urine of Weston during his famous walk, and are occasionally seen in the urine of dyspeptic patients, especially when oxaluria or lithuria is present.

Fig. 5. Deposit from acute catarrhal nephritis showing: *a*, Slender hyaline cast; *b*, Mucous cylinder; *c*, Hyaline and epithelial cast; *d*, Pear-shaped epithelial cells from pelvis of kidney; *e*, Epithelium from tubules.

They are usually slender homogeneous transparent cylinders (*Fig.* 5, *a*), but are often more or less opaque from fatty degeneration, and are then called "granular" casts (*Fig.* 4, *d*).

Various origins are assigned to them, and they are probably formed in three different ways.

Langhans has described a colloid metamorphosis of epithelial casts by which they become wholly or partly hyaline or glass-like in appearance; if the change is only partial they would be called hyalo-epithelial casts (*Fig.* 4, *e*); if complete they form one kind of hyaline cast, which, like the epithelial cast it originally was, is distinguished by its large diameter. In some instances, these transformed casts give the characteristic colour reactions of lardaceous material, turning mahogany-brown with iodine and rose-violet with methyl blue; but not

necessarily in association with or dependent upon lardaceous changes in the blood vessels of the kidney.

The second mode of origin is by coagulation of transuded plasma. Salkowski and Leube suggest that fibrin is formed by the action of the dead epithelium on the fibrinogen of the blood serum. This doctrine has been warmly opposed by the French school, who have pointed out that hyaline casts are physically and chemically differentiated from fibrin; they are non-fibrillated, they do not swell upon the addition of acetic acid, and they are soluble in distilled water, especially when warmed. Fibrin cylinders are sometimes met with, but supporters of the doctrine that hyaline casts, or some variety of them are derived from the blood, ascribe them now to a modification of albumen, effected in some such way as acidulation by the renal epithelium.

Ribbert tied the renal artery of a rabbit for 1½ hours and then injected a weak 2½ per cent. solution of acetic acid into the jugular vein. After boiling the excised kidney he found Bowman's capsules filled with a hyaline mass, and after hardening in alcohol this mass was granular. He also boiled an albuminuric kidney in acidulated water, with the result that beautiful hyaline masses were formed in it; uric and phosphoric acid and hydrochloric acid gave equally good results; but urea did as well, so that acidulation *per se* appears not to be the essential condition. As these casts have been found in kidneys whose epithelium was quite intact, it must be admitted that congestion alone may give rise to them.

Ernst has more recently revived the argument in favour of the fibrinous nature of hyaline casts by showing that they give Weigert's characteristic fibrine staining, but Lubarsch contends that there are many non-fibrinous substances in the body which take up Weigert's stain and in addition hyaline casts may be coloured by agents that will not stain fibrine. Ribbert admits that fibrine cylinders occur under certain conditions, but still believes in the usual origin of these casts from a modified albuminous transudation.

A third theory ascribes them to an exudation or secretion from the tubular epithelium. Aufrecht found after ligature of the ureter in rabbits, if the kidneys were examined within the first three days, the tubules contained many hyaline cylinders, although the epithelium was intact and the interstitial tissue and blood vessels did not show the slightest change; moreover, he once saw a cylinder made up of single irregular pieces,

separated by fine bright lines, and some of the epithelial cells had fine bright rounded structures projecting from them.

Strauss and Germont have recently confirmed this observation by researches made with a degree of care that leaves nothing to be desired.

In thin sections of pieces of kidney hardened in osmic acid, it is seen that even in the first few hours after the ligature the clear protoplasm of the epithelium of the convoluted tubes, and of Henle's loops disappears, and only the striated basal portions with the nuclei remain.

This change is closely connected with the formation of these casts, which three or four days after the ligature are present in great numbers in the convoluted tubules, as well as in the medulla and pyramids. Other tubules may be seen not yet filled by casts, in which the granular contents of the epithelial cells are projecting into the lumen, in the shape of spherical processes of the same colour and consistence as the casts. The following stages in the formation of casts from the exuded droplets can be noted: some are already exuded from the cells and lie free in the lumen of the tube (*Fig.* 6); others project half-way or more and remain still in connection with the cell matrix. Where the change is further advanced, a

Fig. 6. **Convoluted tubule, catarrhal nephritis. Epithelium represented by only basal portion. Cavity of tubule filled with protoplasmic droplets from which casts are formed (osmic acid).**

number of droplets may be seen to group themselves so as to form a cylindrical mass, the centre of which is homogeneous while the exterior is scalloped by the want of coalescence of its spherical components.

It is said by Kelsch that casts formed in this way are composed of a colloid material which exudes from the cells of the

ordinary hyaline cast, by coagulating into a harder and more brittle substance, having a feebly yellow colour, which stains dark brown with osmic acid, and rose-pink with picro-carmine.

There appears to be good reason for accepting the view that hyaline casts originate in each of these ways. It has been already stated that those formed by metamorphosis from epithelial casts, can generally be recognised by their larger size, or by the change being incomplete. Of the other two kinds it is a question which is the more common. On *à priori* grounds we should expect that where there is only congestion the casts should be formed by transudation; but where inflammatory conditions are present, by secretion. If this is really so, the staining reactions given by Kelsch would afford valuable indications.

I believe that casts are very rarely formed by transudation, and my opinion is based on their rarity in so-called functional albuminuria. As a clinical fact we know that casts are only few and far between, unless inflammation is present. We know that in diabetes, when casts are present, there is apt to be structural kidney change; and their presence in jaundice is explained by the observations of Mobius, who found that persistent excretion of bile by the kidneys destroyed the renal epithelium. So, too, in old standing heart disease, the kidneys are liable to more or less change of a chronic inflammatory nature. It is also quite probable that there are transient conditions of renal irritation, comparable with that produced by temporary constriction of the renal artery, in which the epithelium may secrete casts, and that this explains their occurrence in the case of Weston, and in attacks of gout. Practically, therefore, we ought to attach very high importance to the recognition of epithelial and hyaline casts as evidences of irritation or inflammation of the renal epithelium. We can measure the intensity of this process by their number, and watch its progress by their persistence.

Epithelial casts bear witness to severe inflammation, such as occurs in acute and sub-acute Bright's disease; broad hyaline casts have the same meaning, being formed from the epithelial variety as already explained, but slender hyaline casts testify only to a mild inflammatory process, such as occurs in the contracting kidney, or during the subsidence of an acute attack.

Summary.—1. Casts of the renal tubules are of three kinds —blood, epithelial, and hyaline.

2. Blood casts are evidence of hæmorrhage from the glandular substance of the kidney.

3. Epithelial and broad hyaline casts are evidence of acute and sub-acute inflammation of the kidney.

4. Slender hyaline casts are evidence only of a mild inflammatory process, which may be the result of a transient irritation.

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CHAPTER V.

CARDIO-VASCULAR CHANGES.

NEXT to dropsy and the state of the urine, the alterations in the circulatory system are the most striking clinical and pathological facts met with in Bright's disease. Clinically, they are present in the shape of physical evidences of cardiac hypertrophy, with increased arterial tension; pathologically, the changes described are hypertrophy of the heart, and thickening of the small arteries.

The hypertrophy of the heart may be a genuine hyperplasia of the muscular substance, but evidences of interstitial myocarditis, such as thickening of the inter-muscular fibrous tissue, and pigmentary or fatty degeneration of the muscular fibre are often present.

The heart may enlarge very rapidly even in acute nephritis, but it is in association with the chronic forms, especially the contracting kidney, that hypertrophy is most commonly met with. Bartels asserted that he had "never failed to obtain the objective signs of hypertrophy of the left ventricle in any of his cases of genuine contracting kidney, or to confirm the fact in every *post mortem* made upon their bodies, and therefore he can never hold that a diagnosis of this renal disease is made certain when no enlargement of the left ventricle is recognised." This statement would be of the utmost value if true, for we should then have a most important confirmatory sign.

Dickinson says that an analysis of 250 cases of granular degeneration, drawn from St. George's Hospital books, gave 48 per cent. as the proportion of cardiac enlargement, and that since his attention was directed to the subject he has scarcely seen an instance in which, if the renal disease was distinctly recognised, whether after death or in life, some degree of cardiac hypertrophy was not also present. He regards simple cardiac hypertrophy as one of the most important diagnostic signs of this form of renal disease.

Ewald found hypertrophy of the heart in 20 out of 21 cases of granular kidney. On the other hand Grainger Stewart

speaks of nearly one half of a series of cases he examined *post mortem* having had enlarged heart simply from renal disease, while many others had enlargement connected with valvular or vascular lesions.

Gull and Sutton state that they have particulars of nine cases in which the kidneys were very contracted and the heart was free from hypertrophy.

I found that out of 100 typical cases examined *post mortem* at the General Hospital, 44 had simple cardiac hypertrophy, and 16 hypertrophy with valvular disease, the proportion being 60 per cent. of hypertrophy with and without valvular disease. In addition, out of 87 carefully selected living cases in which the state of the heart was noted, and in which the coincidence of symptoms fully justified the diagnosis of contracting kidney, there was evidence of cardiac hypertrophy, with or without valvular disease, in 52,—also as nearly as possible 60 per cent. of the cases.

The following table gives the state of the heart in 807 cases of all forms of Bright's disease collected by Bamberger.

Form of Bright's Disease.	Excentric hypertrophy of the whole heart.	Excentric hypertrophy of the left ventricle.	Simple hypertrophy of the whole heart.	Simple hypertrophy of the left ventricle.	Simple dilatation of the whole heart.	Simple dilatation of the left ventricle.	Total.
Acute - -	3	4	2	2	4	0	15
Chronic -	51	38	3	24	5	1	122
Contracting	88	65	6	39	7	2	207
Total	142	107	11	65	16	3	344

Senator has endeavoured to show that in contracting kidney the heart undergoes concentric hypertrophy, while in fatty kidney the hypertrophy is accompanied by dilatation, causing excentric hypertrophy. Hanot has supported these views. While every pathologist will admit the frequency with which hypertrophy with very little dilatation accompanies contracting kidney, all pathological records disprove such an arbitrary division. Grawitz and Israel found in artificial nephritis, that while the small red or large white kidney resulted indifferently, concentric and excentric cardiac hypertrophy occurred also without any relation to the type of the accompanying change in the kidney, and this is equally true in human pathology.

Traube has the merit of being the first to draw attention to the

hard radial pulse so frequently present in contracting kidney; and this fact, together with the accentuation of the second sound of the heart, has been particularly insisted on by Johnson. Sibson drew attention to the doubling of the first sound often accompanying these two phenomena, and explained all three as evidences of increased blood pressure in the aortic system.

Galabin has shown that the high tension pulse occurs in all forms of renal disease, but is most constant in cases of contracting kidney.

Our present purpose is to enquire into the nature and causes of these changes.

This pulse of high tension can be readily recognised. In some cases the radial artery is hard and prominent, feeling, as has been said, like the spermatic cord, but without any unevenness to suggest calcareous deposit; in other cases there is nothing noteworthy about the feel of the vessel. The compressibility of the pulse can be best estimated by placing the forefingers of both hands side by side upon the artery, gradual pressure being made with the proximal finger, while the distal finger notes the effect upon the pulse.

The sphygmographic tracing of the high tension pulse is characteristic.

Fig. 7 represents a tracing from a normal pulse. The letter *a* is placed at the summit of the percussion up-stroke, which is caused by the sudden impulse of the ventricular systole, and corresponds in height to the force of the left ventricle. The letter *b* marks the dicrotic notch; the little fall is due to the termination of the *systole* and the little rise to the recoil of the

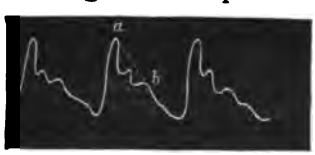

Fig. 7. Normal pulse tracing. *a*, At summit of percussion up-stroke; *b*, Dicrotic notch; *a* to *b*, Tidal wave.

Fig. 8. Pulse tracing, acute nephritis, showing high tension with a relatively feeble ventricle (myocarditis ?).

Fig. 9. Pulse tracing; chronic nephritis, with heart failure. High tension with a relatively feeble ventricle (brown atrophy and incompetent aortic valves).

vessels and the closure of the aortic valves. From *a* to *b* is the curve of the tidal wave, which lies below the straight line drawn from *a* to *b*. The position of this tidal wave line is the

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index of tension; it rises with the tension until in high tension pulse tracings it lies above the line *a b*.

Figs. 8, 9 and 10 are tracings of pulses from three typical cases of Bright's disease. *Fig.* 8 is from acute catarrhal nephritis after sore throat; *Fig.* 9 is from a case of large white kidney which died from heart failure; and *Fig.* 10 is from a well marked case of contracting kidney which led to complete blindness from albuminuric retinitis.

Fig. 10. Pulse tracing; contracting kidney. High tension, with cardiac hypertrophy.

In *Figs.* 8 and 9 the short upstroke is due to the relatively feeble left ventricle. In the acute case there were signs of cardiac dilatation probably caused by acute softening (myocarditis); and in the second case we had *post mortem* evidence of the state of the heart.

Bright, in recording the various organic changes in a hundred cases of renal disease, says, "The obvious structural changes in the heart have consisted chiefly of hypertrophy, with or without valvular disease; and what is most striking, out of fifty-two cases of hypertrophy, no valvular disease whatsoever could be detected in thirty-four; but in eleven of these thirty-four, more or less disease existed in the coats of the aorta; still, however, leaving twenty-two without any probable organic cause for the marked hypertrophy generally affecting the left ventricle. This naturally leads us to look for some local cause for the unusual efforts to which the heart has been impelled; and the two most ready solutions appear to be, either that the altered quality of the blood affords irregular and unwonted stimulus to the organ immediately, or, that it so affects the minute and capillary circulation as to render greater action necessary to force the blood through the distant sub-divisions of the vascular system."

It will be found that the pendulum of modern opinion is now again oscillating between these two explanations in spite of forty years of discussion and observation with the aid which the modern use of the microscope has lent to pathological researches. Thus Senator suggests that in chronic parenchymatous nephritis the hypertrophy is probably attributable to the increased capillary resistance; while, in interstitial nephritis, the hypertrophy is due to direct irritation of the heart, either from some nervous disorder, as in Graves' disease, or, as is more likely, from the blood dyscrasia.

Since the time of Bright there have been four original explanations brought forward and all other writers have adopted some one, or a combination, of these four theories.

Traube, to whom we owe the observation of the hard pulse of Bright's disease, regarded the destruction of a large capillary area in the kidneys as necessarily causing so much obstruction to the circulation that, aided by the imperfect elimination of water, the blood pressure in the aortic system must rise and cardiac hypertrophy follow. Bamberger objected to this that the hypertrophy begins in the earlier stages of Bright's disease; moreover it is present in chronic parenchymatous nephritis in which no destruction of capillaries has occurred. Ludwig and his pupils have shown that ligature of both renal arteries, or of even larger arteries, does not raise the blood pressure in the aorta; while it is well known that in contracting kidney the elimination of water is rather in excess of the normal, yet it is specially in this affection that cardiac hypertrophy occurs. It is, therefore, not without reason that this hypothesis has been generally abandoned, although in recent times it received the support of so eminent an authority as Bartels.

The next original explanation was that given by Johnson, which has undergone at least two modifications. In the first place Johnson pointed out the excessive thickening of the muscular walls of the renal arterioles, and suggested that the obstruction to the circulation offered by a state of tonic spasm in these vessels would explain their own alterations, the rise of blood pressure and the cardiac hypertrophy. But having been able to discover similar changes in the vessels of the pia mater and mesentery, he enlarged his hypothesis and imagined a state of tonic spasm of the whole systemic arterioles which he attributed at first to direct irritation by the impure blood, and later on to stimulation of the vaso-motor centre. According to his latest views he regards the condition as analogous to asphyxia, in which unoxygenated blood going to the brain stimulates the vaso-motor centre in the medulla, and causes contraction of the arterioles throughout the body with consequent increase of the arterial blood pressure. A great objection to this theory of general constriction of the vascular system is that, under such circumstances, the urinary secretion would be diminished or suppressed, as happens in asphyxia (EICHHORST); whereas in contracting kidney, as is well known, the rise in blood pressure is accompanied by an increase in the flow of urine. Grützner has shown that the

diuresis excited by the intravascular injection of salts, such as nitrate of potash, is arrested during suspension of the respiration, unless the nerves to the kidney are divided. There is, however, good clinical evidence that vascular contraction occurs in the *skin*, as shown by the remarkable grey complexion, cold hands and feet, and "dead fingers" so often observed in the subjects of chronic Bright's disease, and it may be fairly allowed that the constant recurrence of this phenomenon would not be without effect upon the heart in the course of time.

The third original explanation is that of Gull and Sutton. They rediscovered the vascular changes described by Johnson, but drew special attention to the thickening of the inner and outer coats, and asserted that the muscular coat was atrophied. They regarded these vascular changes as primary and essential; of which the increased blood pressure and cardiac hypertrophy are results, while the kidney disease is a mere local expression of a generalised degeneration of the arterioles and capillaries, attended by atrophy of adjacent tissues. With regard to these assertions we owe to Thoma the careful measurements which demonstrate that the arterioles of the kidney are absolutely dilated, in spite of the increased thickness of their walls. He showed, too, by careful injections, that while fluids run well into the Malpighian bodies, the efferent artery is often destroyed, and the capillary plexus on the tubules is to a large extent obliterated.

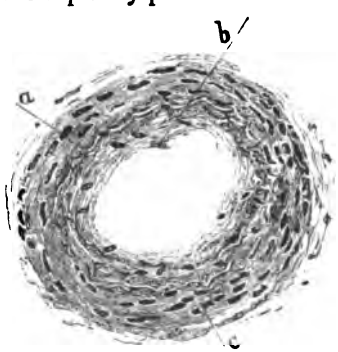

Fig. 11. Renal arteriole showing Endarteritis obliterans. *a*, Swollen elastic lamina, its fibres separated and œdematous; *b*, Broad growth of connective tissue from the endothelial layer; *c*, Swollen muscular coat with large distinct nuclei (contracting kidney).

Moreover, an unprejudiced investigation of sufficient extent will convince any one that many vessels show great hypertrophy of the muscular coat, and that not a few present an appearance of a concentric arrangement of spindle cells lined by swollen elastic tissue (*Fig.* 11). In others, however, the inner coat is much thickened, forming a broad layer of lowly organised connective tissue; the muscular coat may be atrophied, and the adventitia passes inseparably into the surrounding connective tissue.

I have looked for the changes in pia mater, peritoneum, skin and other tissues. In the pia mater, thickened vessels are often seen, in other situations very rarely. But the pia mater

itself is often altered in chronic Bright's disease, looking opaque, and more or less milky. It is in this condition that the thickened vessels are found, and the true interpretation seems to be that it is a chronic endo- and peri-arteritis associated with sub-inflammatory changes in the perivascular tissues.

But, apart from this, the changes are not constant. Ewald found out of twenty cases of contracting kidney with hypertrophied heart, the vessels were not thickened in four, while in a similar examination I found them not thickened in two cases out of ten, so that this disposes of the assertion that the vascular lesion is primary and essential. As, too, in chronic nephritis following an acute infective attack, cardiac hypertrophy is common while the vascular changes are exceptional, they cannot be regarded as standing in any important relation to one another. Finally, we know that both cardiac hypertrophy and high tension pulse occur in acute nephritis and even in "surgical kidney," in which there is no question of "arterio-capillary fibrosis."

The last explanation is that of Buhl. He believes the cardiac and renal changes proceed *pari passu*, the hypertrophy being attributed to the increased activity of the heart. Myocarditis occurs very early, and may lead to no alteration, or to atrophy or hypertrophy of the organ, according to circumstances. Most frequently it causes hypertrophy. As the inflammatory process comes to an end the cardiac muscle hypertrophies from excess of nutrition, and to overcome the increased work of the dilated ventricle. In addition he asserts that a relative stenosis of the aorta is present. The rise of blood pressure in the aortic system is therefore due to the hypertrophy of the ventricle and the narrowing of the aorta.

The relative frequency of myocarditis in renal disease is an undoubted fact, and this process plays an important part in many cases, but there is no warrant for the assumption that it has occurred in all cases. Buhl is not at all clear as to the cause upon which the increased activity of the heart or the myocarditis depends. He cannot claim novelty for the fact that the aorta is in some cases relatively stenosed, for Bamberger adduced it as opposed to Traube's hypothesis. With regard to its frequency in granular kidney Ewald has measured the circumference of the aorta above the valves in twelve cases, and found it to vary between 12·1 and 5·7 cm.,

the average being 7·6 cm., while the normal circumference according to Bouillaud is 6·3 cm., so that very much importance cannot be attached to it as a cause of cardiac hypertrophy.

Having failed to find any of these explanations quite satisfactory, let us return to Bright's suggestions, either that the altered quality of the blood affords irregular and unwonted stimulus to the heart immediately; or, that it so affects the capillary circulation as to render greater action necessary to force the blood through the distant subdivisions of the vascular system. Both these explanations rest upon the supposed impure state of the blood. In the acute and chronic stages of parenchymatous nephritis the condition of the blood was investigated many years ago by Bostock, Gregory, and Christison. According to the latter, urea was always found in considerable quantity in the blood whenever the excretion of urine was diminished; the density of the blood serum was always less, and the fibrine was frequently increased. Nothing of importance has been added to this observation in modern times; but experiments with animals have shown that urea, extractive matters of the blood, creatine and leucin accumulate in large quantities in the blood and tissues after nephrotomy; and it cannot require much argument to convince anyone that during the abeyance of the renal function the blood depurating process must be more or less incomplete.

In contracting kidney the density of the serum is diminished (REES, RAYER); the proportion of salts and albumen is lowered; and there is a rapid reduction of the blood pigment or hæmoglobin (LEICHTENSTEIN). Bartels published some observations, but none of them bearing on the state of the blood in the earlier stages; in the later stages, when dropsy was present, the density of the blood serum was low; a certain amount of urea was found in many cases, in others it was absent.

There are other reasons for believing that blood impurities are early and important phenomena in contracting kidney. Todd first pointed out the frequent co-existence of this form of renal disease with gout, hence the name gouty kidney; Ollivier has drawn attention to its common occurrence among workers in lead. Johnson states that the disease is common in persons who "eat and drink to excess, or who, not being intemperate in food or drink suffer from certain forms of dyspepsia, without the complication of gouty paroxysms." He says that "renal

degeneration is probably a consequence of the long-continued elimination of products of faulty digestion through the kidneys." Murchison was persuaded of the relation borne by contracted kidney to persistent lithæmia. Semmola, of Naples, maintained the view that Bright's disease is a consequence of the blood dyscrasia resulting from suppression of the respiratory function of the skin.

Therefore, although during the greater part of its course this affection does not lead to any diminution of the renal secretion, there is ground for believing in a blood dyscrasia depending upon other causes.

The next point for inquiry is whether such blood impurity as may arise from defective elimination or perverted digestive functions can be shown under any conditions to obstruct the capillary circulation. Heidenhain speaks of copious diuresis occurring after the injection of urea in spite of the blood pressure remaining below normal, or not being proportionately increased.

Ustimowitsch and Grützner after injecting urea into the blood observed a certain constant rise in blood pressure accompanied by increased flow of urine.

Rendu in his inaugural thesis quotes Potain as having noticed that although injections of urea into the blood do not modify the mechanical conditions of the circulation, yet if a mixture of urea and blood serum be allowed to stand some hours, and be then injected, the arterial tension rises to an unexpected degree.

Haig finds that retention of uric acid in the blood causes increased vascular tension, but he considers that the effect is produced by the intervention of some modified albumens resulting from the dyscrasia.

Grawitz and Israel found that neither unilateral artificial nephritis nor extirpation of one kidney, although followed by hypertrophy of the heart, effected any rise in the blood pressure. By taking strict antiseptic precautions they were able to clamp either of the renal arteries of a rabbit without any unfavourable surgical result. One and a half to two hours afterwards the clamp was removed. In half an hour after the operation the urine became bloody, and in from one to two hours the organ if examined was found to be greyish red and opaque. If the clamp was allowed to remain on longer the kidney became of a dirty yellowish grey colour, indicating commencing gangrene. The effect of this operation was to

cause intense acute parenchymatous nephritis with fatty degeneration of the epithelium of the tubules. This passed into either granular atrophy or the large white kidney. In the former, microscopical examination showed no trace of nuclear prolification, the substance of the organ consisting simply of wasted tubules. In another series of experiments they extirpated one kidney altogether. They found that the results of these conditions varied accordingly as the animals operated on were young and growing, or old, strong, and fully grown.

In young animals, after two or three days, the intact kidney began to increase in size to 20 or 30 per cent. more than its normal weight. As the contraction of the other kidney went on, the intact organ continued to increase until it equalled the weight of the two kidneys of an animal of the same size. At the same time they ascertained by abdominal section that the other kidney still secreted a watery urine of low specific gravity, but in small quantity.

In old animals the intact kidney also increased a little, the greatest being in one case of nephrotomy, where the extirpated right kidney weighed 7·7 grms., and the left, after 82 days, weighed 11·3 grms. The hypertrophy of the kidney consisted in a true hyperplasia of the renal elements, at least the enlargement was certainly not due to increase in the diameters of the tubules. The consequence of the imperfect compensation by hypertrophy of the other kidney caused in some cases death by acute or chronic uræmia; in others the animals continued to live, but were ill nourished until the deficit was covered by hypertrophy of the left ventricle.

By careful estimations of the relative normal weights of the heart and kidneys, and comparison of these data with the weights of the altered organs, they were able to determine that the cardiac hypertrophy bore a definite proportion to the loss of renal substance, and therefore was truly compensatory for the renal defect. As a rule the heart was not dilated, in many cases the ventricle was in a state of spasmodic contraction, and they were unable to obtain any confirmation of Senator's views already quoted relative to the pathogenesis of excentric and concentric hypertrophy.

In those cases where cardiac dilatation occurred, the symptoms during life indicated that compensation was either primarily defective or later destroyed, and the animals died with acute or chronic dropsy. In the case of a large black

doe, which died with dropsy of all the serous cavities ten days after the operation, the cardiac muscle was intensely granular, even after the addition of soda solution. They regard this as evidence of the occasional occurrence of *primary* myocarditis. Much more frequently the myocarditis was secondary, but whichever it was it produced the appearance of "excentric hypertrophy." They were never able to obtain evidence of any increased blood pressure, but by careful measurements they determined a constant increase in the velocity of the circulation. Injections of urea also failed to produce a rise of blood pressure, but *stimulated the heart's* action and quickened the blood stream.

More recently Grawitz has shown that cardiac hypertrophy may be induced by loading the blood with urea by giving it to rabbits in their food.

Here we have the explanation of the "self increased activity" of the heart, to which Buhl refers, and also of the myocarditis. The impure state of the blood acts as Bright suggested, by affording an unwonted stimulus to the heart immediately, and this leads to a hypertrophy proportionately compensating for the loss of renal secreting substance. Myocarditis is the cause of dilatation and the subsequent hypertrophy takes place as Buhl indicates, from over nutrition and increased work due to the greater capacity of the ventricle. The rise in blood pressure is not a cause of the cardiac hypertrophy, but a consequence; yet in these experiments the state of the heart, the renal condition, and the blood impurity combined, were unable to effect any increase in the tension of the aortic system.

But the high pressure pulse of Bright's disease is a constant and now universally admitted fact. Traube asserted, not without reason, that he could diagnose contracting kidney by the pulse alone, and Galabin has shown that the same condition is present in the other forms of Bright's disease. A great step was taken when Mahomed proved that this rise in blood pressure precedes the occurrence of albuminuria, the development of which he watched at the termination of scarlatina. Here there is no question of structural change in the heart or arterioles; the sole condition present is that of faulty elimination due to the morbid state of the skin. When constipation occurs the blood pressure rises, and if not averted by a sharp purge, albuminuria follows. Moreover, Mahomed recorded cases of high arterial tension, sometimes accom-

panied by albuminuria, in young dyspeptic patients free from cardiac hypertrophy.

If the rise in pressure precedes all structural change it must be due to increased energy in the cardiac contractions, or to obstruction in the distant parts of the vascular system, or to both combined. Most modern writers, Grainger Stewart, Broadbent, Mahomed, Ewald, and others, regard the obstruction as seated in the capillaries, and the cardiac hypertrophy as the consequence of this impediment to the circulation. But we have seen that the cardiac hypertrophy must be regarded as directly dependent on the state of the blood, and therefore is rather to be regarded as a cause than an effect of the rise in blood pressure.

Grawitz and Israel appear to have proved that the cardiac hypertrophy *per se* does not raise the blood pressure, nor does the state of the blood which manifests itself by the stimulus to the heart's action seem to suffice to produce any peripheral obstruction great enough to cause this result. We are compelled therefore to seek some other factor, or to believe that in some respect the conditions of these experiments differ from those of patients suffering from Bright's disease. Such a difference plainly existed in the intact state of one kidney, and it may be that the rise of blood pressure, with which we are clinically familiar, is the result of a dyscrasia differing in some respects from that present in these experiments.

Hamilton has suggested that the increased capillary resistance may be explained by alterations in the specific gravity of the blood serum, and gives the following ingenious explanation of the way in which obstruction would be effected by this change.

Any one who has watched the circulation of the blood in a frog's web or mesentery, has noticed the way in which the corpuscles run in a central core in the blood vessels. "This is due to their being of almost exactly the same specific gravity as the serum. If a body of the same specific gravity as the liquid in which it is suspended is made to travel through either a straight or bent tube, it runs in the axial stream, while, if it is lighter or heavier than the liquid it runs respectively on the upper or lower surface of the tube. The coloured blood corpuscles are almost of exactly the same specific gravity as the *living* plasma in which they are suspended, while the colourless are markedly lighter. Now the whole essence of the blood as a circulating fluid, is that the coloured corpuscles suspended in

it never touch the wall of the smaller vessels, even of the minutest capillaries. They glide along in the axial stream without any sign of impediment. A body of the same specific gravity as the liquid in which it is suspended further turns round a curve in the tube with ease, while one lighter or heavier experiences the greatest difficulty in doing so and continually tends to catch at the bends.

"Hence from the great mass of the solid particulate matter of the blood being practically of like specific gravity with the living plasma, undue friction is avoided, and the blood as a whole circulates with very much the same facility as pure plasma would. When a light substance such as oil or milk is introduced into the circulation it will not circulate, because the particles catch in the curves of the vessels, more especially in parts like the lung, where the vessels are particularly tortuous. Blood circulates through a capillary glass tube exactly as it does through a small vein or capillary vessel. The coloured corpuscles occupy the axial stream, the colourless the peripheral. Hence the phenomenon must be a purely physical one. Further, the position in the stream occupied by bodies thus suspended in a liquid may be altered at will, not only by altering the specific gravity of the bodies themselves, but also by changing that of the suspending liquid.

"Thus by substituting a very light liquid or a very heavy one, the suspended blood corpuscles may be made at will to course along either the lower or the upper surface of the vessel. They come in contact with it, and by rubbing against the wall are made to roll instead of to glide. The friction thus caused retards their progress; they tend like oil globules to catch in the curves of the vessels and thus to cause obstruction to the ever continuous flow of the blood stream. The difficulty that may thus be caused by this apparently trivial cause in moving the blood onwards, comes to be very great when estimated all over the body; and were it the case that a marked difference in the relative specific gravities of the blood plasma and the coloured corpuscles prevailed, the continuance of the even onflow of the blood with the usual propelling power would become a physical impossibility."

I have made this long quotation in order to secure the advantage of the author's own words, as the explanation is exceedingly interesting and ingenious, and has not received the attention it deserves.

Summary.—1. Cardiac hypertrophy is met with in all forms

of Bright's disease, including acute nephritis, but is most common in contracting kidney.

2. It is due to: (*a*) stimulation of the heart to increased activity by the presence of non-eliminated poisonous matter, *e.g.*, urea, in the blood; (*b*) increased capillary resistance.

3. Increased capillary resistance may be ascribed to alterations in the density of the blood plasma.

4. The high tension pulse is due to the same causes: viz., increased energy of the heart and greater capillary resistance.

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CHAPTER VI.

PATHOLOGY OF POLYURIA.

IN the later stages of acute Bright's disease the urinary secretion, which is greatly diminished at the commencement of the attack, often rises to more than the normal amount; in chronic parenchymatous nephritis the daily quantity of urine is generally excessive, while in the contracting kidney Christison wrote truly "No single symptom has appeared to be so invariable or of so much service for indicating the commencement of the disease as the fact of the patient being awakened once or oftener in the night time by the necessity of passing urine. I have scarcely ever known it wanting when any other local symptom existed; frequently it has been present without any other for a great length of time, and it is so remarkable a deviation from the ordinary rule of health that, although it may have been neglected, no individual can fail to recall it when his memory is tasked on the subject by his physician."

This copious urine is after all a poor secretion, often containing less than the normal total solids, and represents solely an increase in urinary water.

The question how this increased outflow of water is caused may not appear at first sight a very practical one, but it has an important bearing on prognosis and treatment, and its theoretical interest is evidenced by the attempts of most authors to give some satisfactory account of it. Thus Bartels gave the following explanation:—

"Observation teaches us that contracting kidneys which have dwindled down to more or less considerable remnants of secreting glandular tissue, do not merely continue to secrete urine, but in the large proportion of cases actually furnish, in the same interval of time, a larger quantity of urine than healthy kidneys would supply. This, however, takes place only so long as the condition of the hypertrophied left ventricle is capable of maintaining the blood pressure in the aortic system at its abnormal height. That the secretory performances of the kidneys depend upon the elevation of the pressure

in the arterial system, is proved as distinctly as is possible by physiological experimentation. If the arterial pressure exceeds its normal bounds, it follows of necessity that, *cæteris paribus*, a larger quantity of urinary fluid must be forced through the renal apparatus during the same interval of time than would take place under normal pressure." . . . . "The greater rapidity with which the secretion of the urine is conducted is, at the same time, the cause of its possessing so invariably low a specific gravity, *i.e.*, of its remaining so relatively poor in solid constituents." . . . . "But so soon as the propulsive power of the hypertrophied heart is reduced, in consequence either of some temporary or permanent influence, the abnormally large amount of urine falls off and the abnormally low specific gravity rises."

On the other hand, Johnson takes a different view; he says, "There is no reason to suppose that high arterial tension has any direct tendency to cause an increased secretion of urine. In cases of contracted kidney the two conditions are associated, but in the early stages of lardaceous kidney the copious secretion of urine occurs without arterial tension. It is probable that in both classes of cases the copious flow of urine is caused by the diuretic influence upon the kidney of some abnormal products in the circulation,—an influence analogous to that of sugar in diabetes." But it is also part of Johnson's theory that the renal arterioles are contracted; in his own words, "The contraction of the hypertrophied renal arterioles counteracts the injecting force of the strong left ventricle, and thus prevents an afflux of blood in the capillaries of the kidney."

Grützner found that when he injected saltpetre into the blood, the renal nerves on one side only being divided, the urinary secretion was copious, and equal from both kidneys, when there was only a slight rise in the blood pressure; but when the latter was artificially raised by suspension of respiration, the secretion of urine sank in the kidney with its nerves undivided. That is to say, the saltpetre produced its diuretic influence on both kidneys so long as the flow of blood to them was unimpeded, and without the aid of a general rise in the blood pressure; but the moment the arterioles were contracted under the influence of the vaso-motor nerves stimulated into action by the poisonous effect of the carbonic acid upon their centre in the medulla oblongata, the urinary secretion continued only from that kidney whose arterioles, by division of their nerves, were beyond the reach of vaso-motor action.

Newman has suggested that the polyuria of contracting kidney is due to obstruction of the lymphatics.

Physiologists are now agreed that the *amount* of urine depends for the most part upon the blood pressure in the area of the renal artery; this may in turn depend upon (*a*) Systemic causes, by which the general blood pressure is raised; (*b*) Local causes, determining the afflux of blood to the glomeruli.

The last chapter was devoted to the subject of the high arterial tension of Bright's disease, and to proving that this is due to two factors—(1,) The over activity of the heart stimulated by the presence of excrementitious matters (urea, urates, etc.,) in the blood, and (2,) Impeded capillary circulation from alterations in the blood serum. It is unnecessary to repeat the facts and arguments of that chapter. In the general rise of blood pressure there is the first and most important factor in the causation of polyuria, for nothing can be more certain than the clinical fact already alluded to by Bartels, that as in the later stages the heart fails, the polyuria disappears and dropsy sets in.

Temporary plethora produced by abundant drinking is rapidly followed by polyuria.

In the large white kidney, the renal vessels are *dilated* from inflammation, so as to favour the access of a large amount of blood to the Malpighian bodies; this in part accounts for the polyuria in this form of Bright's disease.

In early cases of contracting kidney there is nothing to oppose the free afflux of blood to the glomeruli, while the progressive destruction of capillary areas beyond them must tend to raise their blood pressure and favour filtration. But in the advanced stages of contracting kidney the renal artery is, according to Thoma, narrower than normal; this is probably counterbalanced by the reduced number of glomeruli to be supplied, and we know from the same observer that the arterioles are dilated, so that the afflux of blood to the glomeruli is very free. We may therefore conclude that there are local conditions which favour the occurrence of high pressure within the glomeruli.

But hydrostatic pressure alone is not concerned; the epithelial cells covering the glomeruli participate in the process of secretion. It is to this factor that Johnson ascribes the polyuria. Heidenhain found that a copious flow of urine followed the injection of urates into the blood, while the blood

pressure remained low; and urea is said (LANDOIS) to owe its diuretic action to its influence on the epithelium, though Ustimowitsch and Grützner observed the polyuria produced by it to be accompanied by increased arterial tension,—a result we should expect from what we have learnt previously of its action in stimulating the heart's energy. Munk says that all ordinary diuretics, except digitalis (*e.g.*, common salt, sugar, caffeine, saltpetre, glycerine, pilocarpine) cause diuresis by their direct effect on the renal epithelium, as they widen the renal arteries and slow the blood current. Finally, differences in the permeability of the glomerular walls must also be held accountable for changes in the amount of urine. Thoma found that in very early stages of the contracting kidney, before the microscope shows any changes in the glomerular wall, this structure becomes abnormally permeable. We may assume a similar increased permeability as being probably present, though this has not been proved, in the large white kidney.

Summary. Polyuria is due to the co-operation of these four factors :—

(*a*) Increased general blood pressure; explained in the last chapter.

(*b*) Increased local blood pressure; due to dilatation of afferent vessels and destruction of capillary areas beyond the glomeruli.

(*c*) Increased activity of the glomerular epithelium, stimulated by the presence of urea, urates, etc., in the blood.

(*d*) Increased permeability of the glomerular walls.

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CHAPTER VII.

PATHOLOGY OF URÆMIA.

URÆMIA is the name usually given to certain disturbances of the nervous system arising in the course of Bright's disease and in other serious renal disorders.

There are three types under which these phenomena may be grouped. In one the patient lies in a typhoid condition with a dry tongue and feeble pulse, often vomiting, but showing no disturbance of intelligence or special sense, without convulsions or any loss of consciousness that could be called coma. Such cases are met with in bladder diseases and in obstructive suppression of urine. In the more common type there are a moist tongue, headache, sometimes loss of vision, sometimes sudden deafness, or persistent hiccough, vomiting and diarrhœa, persistent dyspnœa, skin eruptions, hyperæsthesia of skin, tremor, twitchings, Jacksonian epilepsy, convulsions and coma. This is the classical type of uræmia associated with Bright's disease.

In yet a third type there may be convulsions and coma, preceded by epigastric pain, with rapid pulse and deep sighing respiration. This resembles that form of coma met with in diabetes, called "Küssmaul's coma," but it has been described by Riess in eight cases of pure anæmia, in five cases of anæmia with renal disease, and in four cases of gastric and hepatic cancer. Senator has observed it in chronic cystitis, gastric cancer, anæmia and atropine poisoning.

Roberts gives "slow panting and laborious breathing" among the symptoms of obstructive suppression of urine. As this type is little known the following case is of interest.

CASE 1. Harriet B., aged twenty, was admitted into the General Hospital, on Sept. 6th, 1884, complaining of severe pain in the left hypochondrium, which came on suddenly fourteen days before and had continued ever since. This was attended by vomiting and purging. On the night of admission there was some epistaxis, which did not recur. Ten months ago she had typhoid fever, for which she was an in-patient at the Queen's Hospital, and she stated that she had never been well since. When she was five or six years of age she had scarlatina, but

could remember no other illness. On admission she appeared an anæmic girl with an anxious expression of face. She complained of lancinating pains in the region of the spleen. On examination the tenderness was too exquisite to permit of very exact exploration; but there was evidently a resistant mass occupying the whole of the left hypochondrium. The heart, lungs and liver were apparently normal. Her tongue was moist, streaked with brown and white paste, but clean in the centre. Her bowels were relaxed, with about three motions in twenty-four hours. She vomited two or three times daily. Her urine amounted to about twenty ounces daily, it was albuminous, and contained a little pus, but no sugar. The needle of an aspirator passed into the swelling failed to withdraw any fluid. The day after admission the quantity of pus in the urine increased very much, so as to constitute nearly half a column of deposit in the urine glass.

September 9th, at 8.0 a.m., she had a convulsive attack which lasted five minutes, and she afterwards passed into a semi-comatose condition. When seen at 10.25 a.m., she was lying apparently insensible, but on being shouted to opened her eyes and turned her head. Her eyelids were partially open; there were sordes on the teeth and lips. Her pupils did not react to light, but the conjunctivæ were sensitive to touch. Pulse 120. Respirations 24, *deep and sighing*. On auscultation, air could be heard entering freely into the thorax. The nurse said that just before the convulsions she complained of *pain in the stomach*. 4.0 p.m.—Pulse 132. Respirations 28; noisy; slightly delirious, crying out occasionally. At 6.30 p.m., the house surgeon, Dr. Morrison, saw her, at the request of the house physician's assistant, with the idea of performing venesection. He found her with sighing respiration, pulse small and scarcely perceptible. Every now and then she moaned "Let me die." Temperature 97°. At 6.45 p.m. she was pulseless, and apparently *in articulo mortis*. A vein at the bend of the right elbow was opened and 24 ounces of a solution of sulphate of soda in distilled water injected. The fluid was neutral, sp. gr. 1018, at a temperature of about 100° F. The apparatus consisted of a glass funnel connected with a fine pointed pipette by rubber tubing. This was first filled with fluid, and the pipette was then inserted into the vein and the funnel raised. By this means a steady flow into the venous system took place. Within a few minutes the pulse returned at the wrist and the breathing became deeper. After 24 ounces were injected, the fluid in the end of the pipette was reddened from the blood and fluid mingling; the flow was then stopped and the arm bound up. The patient revived, became conscious and spoke; said she was thirsty and drank some milk. Temperature 98·6°. At 7.45 p.m. about a drachm of foul urinous pus was drawn off by the catheter. She died at 10.25 p.m., about fourteen hours after the convulsion.

During the last thirty-six hours of her life her temperature was taken every hour. Before the convulsive attack it ranged between 98° and 99·5°. At the time of the attack it was 98·5°, it then rose steadily, till at 10.0 a.m. it had reached 100·6°, falling again by 12 noon to 98°, and, as mentioned above, when Dr. Morrison saw her at 6.30 p.m. the temperature was only 97°. After the operation it rose to 98·6°, and this was maintained at the last recorded time, 9.0 p.m.

At noon on the day of her death, as she had passed no urine since the night, a catheter was introduced into the bladder and about six ounces were drawn off. It was examined the following day by myself. My note

taken at the time says: Colour reddish brown, putrid, alkaline, deposits one-third column of pus; sp. gr. 1011. *Gives a deep brown colour with ferric chloride* not diminished by heating. Albumen about one-third column. No sugar. Deposit under the microscope consisted of granular cells, squamous and pyriform epithelium, bacteria and blood corpuscles.

On the following day a careful *post-mortem* examination was made by Dr. C. E. Purslow, who kindly favoured me with the following notes:—

External appearances.—The body was that of a young woman. *Post-mortem* rigidity was well marked in the lower extremities. There was a small incision in the fold of the left elbow, and the mark of a puncture in the left lumbar region. *Head.*—There was slight increase of the sub-arachnoid fluid, but otherwise the cranial contents were normal. *Thorax.*—The *heart* weighed 9½ oz. The left ventricle was slightly hypertrophied. Both *lungs* were congested and œdematous, and the lung tissue was friable. The *blood* was very watery, with no disposition to clot. (The result of the intra-venous injection resorted to just before death.) *Abdomen.*—The *liver* weighed 43 oz., and appeared normal. The *spleen* weighed 6½ oz., but was otherwise normal. The *stomach* showed signs of chronic catarrh. The right *kidney* weighed 1¼ oz. only; its ureter was patent; its pelvis was dilated and contained a calculus the size of a pea. The medullary and cortical substances were indistinguishable, and together measured only a quarter of an inch in breadth. The capsule stripped off readily.

In the left hypochondrium there was a large mass, on the upper surface of which, and adherent to it, were the duodenum, pancreas, and descending colon. The surface of the mass was purple coloured, and the colon over it also appeared to have blood extravasated under its mesentery and peritonæal investment. On removing the entire mass it weighed 38 oz. At the upper part there was a cyst the size of an orange, containing purulent fluid, which was accidentally ruptured. On section it was composed of an external cyst wall within which was a mass of recent blood clot; inside this was the left kidney in a condition of saccular dilatation. All normal kidney structure was absent. The pelvis contained an irregularly shaped calculus the size of a bean, and another smaller calculus lay in one of the saccules. The *ureter* was dilated but patent. The *bladder* was not enlarged, or its walls hypertrophied. Its mucous membrane was dark coloured, and presented several wart-like outgrowths about one line in height, with rounded surfaces. The *uterus* and *ovaries* were quite normal.

It is very hard to explain these differences in the clinical phenomena of uræmia on the assumption that the simple retention of urea in the blood is the cause of all of them.

When we go a step further and enquire into the various theories that have been propounded to explain these phenomena, we find our difficulties increase.

These theories may be divided into two groups: (*a*) Mechanical, (*b*) Chemical. In the first group, Owen Rees, Traube, and Rilliet attributed the nervous phenomena to œdema of the brain, dependent upon the watery condition of the blood and the increased blood pressure; this has been

supplemented by Rosenstein, who has suggested that the initial change is spasm of the cerebral blood vessels leading to convulsions by cutting off the blood supply, and followed by effusion of serum into the lymph spaces of the brain. Plainly such a hypothesis involves the necessity for some toxic agent to stimulate the vaso-motor centre, so that it brings us ultimately to some sort of chemical theory ; but the fact that the brain is œdematous is disputed by many.

Carter, of Liverpool, in the Bradshawe Lecture for 1888, gives the results of his actual determination of the amount of water present in the brains of two patients dying of uræmia. In one case twenty grammes of partly white and partly grey matter were taken from the middle lobe, carefully dried for forty-eight hours at 82° C. over sulphuric acid, then pulverised and dried again in a similar manner until weight was no longer lost. The weight when the drying was complete was 4·15 grammes. The fluid part therefore equalled 15·83 grammes ; the percentage proportions being 79·25 water to 20·75 solids, or almost exactly those of normal brain substance, namely, 80 water and 20 solids. In the second case the brain was examined in exactly the same way, and the percentages were 74·55 liquid and 25·45 solids, the water being actually less than in normal brain. The value of these figures is perhaps lessened by the fact that fluid leaves the tissues and drains into the lymph spaces after death, so that fluid which may have been in the brain substance during life may have drained into the ventricles before the examination was made. But Bartels reported several cases of uræmia in which he had noticed absence of cerebral œdema, hypertrophy of the heart, and variations in the density of the blood serum.

The chief chemical theories are :—(1,) That it is due to urea in the blood, hence the name uræmia, originally given by Piorry, and accepted by Christison. This theory is the one which has managed to hold its ground, although numerous experimenters have failed to produce any toxic phenomena by the injection of urea into the blood of animals or by making them ingest quantities of urea with their food.

Peabody has calculated on data obtained by experiments on dogs that at least 1½ lbs. of urea would be required to prove fatal, whereas in the body of a man dying of uræmia only ·009 lb. could be recovered. According to Gréhant and Quinquaud the quantity of urea required to produce convulsions in dogs is from $\frac{1}{100}$th to $\frac{1}{80}$th of their body weight, confirming Peabody's estimate.

In uræmia the amount of urea found in the blood has varied from ·2 to 1 per cent. Vierordt estimates the total quantity of blood in man to be 5062·5 grammes or about $\frac{1}{13}$th of the body weight, so that even the highest estimate, 1 per cent., would only give about 1½ oz. instead of the requisite minimum of 1½ lbs.

Snyers found that he could inject into a dog doses of urea equivalent to the amount it would eliminate in three days without producing any ill effects.

Cases have been described by Owen Rees, Christison, Bright, and Frerichs, in which the blood contained large quantities of urea without giving rise to any symptoms of uræmia. Biermer has published a case of anuria lasting 118 days without uræmic phenomena These appeared after the urine began to flow.

Moreover, uræmic symptoms may supervene in spite of the elimination of a normal quantity of urea; such cases have been reported by Rosenstein, Christison, and Liebermeister.

CASE 2. Emily M———, aged 28, was admitted August 7th, 1888, with headache, vomiting, and hæmaturia. She had no dropsy, but her urine, which was persistently albuminous, contained numerous epithelial and hyaline casts. She suffered constantly from frontal headache, and had frequent cramps and vomiting. The urine generally averaged 35 oz. daily. On a diet of fish, chicken, milk, bread, butter and tea, she still complained of these uræmic symptoms, but the quantity of urea eliminated was 450 grains in 24 hours, the percentage being as high as 3·2.

(2,) This urea theory was slightly modified by Frerichs and Treitz, who suggested that the urea, itself innocuous, became converted, under the influence of a peculiar organised ferment, into carbonate of ammonia.

This theory is based upon (*a*,) The facility with which this transformation is effected; (*b*,) The resemblance of the symptoms produced by the intravenous injection of carbonate of ammonia to those of uræmia; (*c*,) The presence of carbonate of ammonia in the blood of uræmic patients.

Researches made to determine the point whether carbonate of ammonia is really present in the blood in uræmia have attained very contradictory results. Snyers states that the blood of dogs some days after the ligature of both ureters contains only traces of ammonia.

Rommelaere concludes that the quantity of ammonia in the blood is increased after nephrectomy; that the quantity is too small to explain the occurrence of uræmia; but that in a few hours after death a large quantity of ammonia is formed in the blood.

(3,) Schottin in 1853 suggested that the extractives of the blood,—creatin, creatinin, leucin and tyrosin were the real poisons.

In support of this Oppler found a great excess of creatin in the blood of nephrectomised animals, and Hoppe-Seyler found a great accumulation of extractive matter in the blood of a patient who had presented uræmic symptoms in the course of an attack of cholera.

(4,) Gauthier has suggested that ptomaines may be the poisonous substances.

(5,) Feltz and Ritter in 1881 commenced a new series of researches which led to unexpected results. They determined (*a*,) That the intravenous injection of fresh urine causes convulsions, coma and death; (*b*,) That their results were independent of the increased pressure produced by the injection or of the organic constituents; (*c*,) That the inorganic constituents injected separately produced the same symptoms as the urine itself, and that of these the potassium salts showed the most powerful toxic action.

Astaschewsky published about the same time experiments supporting these conclusions.

There is no doubt of the toxic properties of potassium salts, but Bouchard and Snyers believe that they do not play so exclusive and preponderating a part as Feltz and Ritter affirm.

In the blood of two eclamptic women in Braun's wards at Vienna, Snyers found in one 2·07 parts of potash per thousand, and in the other 2·06 per thousand, a quantity rather less than the normal amount.

On the other hand, Lépine found in some experiments on animals by temporary compression of the renal artery, that the urine secreted by the injured kidney showed diminution of its solids chiefly in phosphoric acid and potash, while the chlorides were not diminished, but rather increased.

(6,) Bouchard accepts the position that the urine is itself poisonous, but attributes this to various sources: (*a*,) Food derivatives, especially potash salts; (*b*,) Products of intestinal putrefaction absorbed with the blood; (*c*,) Admixture of bile, saliva, and other secretions; (*d*,) Products of tissue metamorphosis.

Voit says, "Symptoms of disease originate wherever any substance which does not belong to the economy accumulates within the body and is not eliminated from it;" and he shows that even sulphate of soda may be deleterious under such cir-

cumstances. The toxic effects are the result of interference with the normal exchanges which take place between the blood and the tissues, and upon which the vital phenomena of the latter depend.

(7,) Lépine has shown that febrile urine is very much more poisonous than non-febrile urine; and Bouchard observed that the day urine is more poisonous than that of the night. The urine in certain diseases is especially poisonous, *e.g.*, pernicious anæmia, jaundice, cancerous cachexia, chronic Bright's disease, etc.

(8,) Rademaker has found urethane in albuminous urine and suggests that this powerful narcotic may be the cause of uræmic coma.

We are not in a position at present to explain precisely the pathogenesis of so-called Uræmia. It is plain that the clinical phenomena vary, and that there are many poisons to which these symptoms may be due.

Since the case of Harriet B. was published (1884), the doctrine that Küssmaul's coma is due to the presence of an acid in the blood has gained ground; it is extremely probable that some cases of uræmia are due to this cause, although the acid has not yet been identified. Carter, in his Bradshawe lecture, relates a case of coma with sighing respiration and "decidedly acid" blood. The acid is probably formed in the intestine, and thence absorbed into the blood.

If we are to get a nearer knowledge of these problems, it must be by differentiating the clinical types, and by recognising the probability that different agencies may be at work in each; moreover in one we may see the effects of a sudden large dose, in another of chronic intoxication.

Summary.—(1,) Uræmia is a convenient generic name given to a large series of nervous accidents which occurs in Bright's disease.

(2,) Its causes must be looked for in certain toxic agencies arising in the blood, in the tissues, or in the intestines, which have not at present been identified with certainty.

(3,) Normal urine contains a certain proportion of some of these poisons, so that its retention is liable to cause them to accumulate in the blood. In disease, these or other poisons may be present in greater quantities with proportionately more serious results.

(4,) Poisons are known to be formed in the intestines; when constipation is present this process is facilitated, and

opportunity is given for their absorption into the blood. Moreover, the intestine forms a channel by which elimination may take place when the renal function is depressed, so that failure of intestinal action is a grave additional danger in Bright's disease.

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CHAPTER VIII.

RETINAL CHANGES.

AMAUROSIS, or defect of vision in association with dropsy, was noticed by Wells, in 1812; but the first actual observation of retinal change in connection with Bright's disease was made *post mortem* by Türck, in 1850.

The visual defects associated with Bright's disease are divided into two classes: (1,) Those due to uræmic poisoning, in which the visual centres in the brain are chiefly at fault; and (2,) Those due to structural changes in the optic nerve and its retinal expansion.

The so-called uræmic blindness of the former class is generally unattended by any changes in the fundi; but Dobrowolsky has observed transitory œdema of the discs, while Litten has noticed that in uræmic attacks there is swelling and cloudiness about the disc.

In the second class the changes observed in the retina may be enumerated as follow: (1,) Diffused opacity from œdema; (2,) White patches, of which there are two kinds—(*a*,) rounded soft-edged areas of exudation; and (*b*,) smaller bright radiating streaks or specks; (3,) Hæmorrhages; (4,) Optic papillitis; (5,) Diffused retinitis, in which many of these may be combined; (6,) Atrophic changes secondary to inflammation; and (7,) General retinal periarteritis.

Apart from the slight changes which occur in acute uræmic poisoning, no retinal affections are met with in primary acute nephritis, though they are liable to supervene rapidly in the acute attacks which so commonly occur in the course of chronic Bright's disease.

They are most frequent and characteristic in the contracting form, and it is to this that most of the recorded observations refer. It has been disputed whether they ever occur in the lardaceous kidney, and this point has been settled in the affirmative; but as what is often called lardaceous disease is merely chronic Bright's disease—*plus* lardaceous degeneration—it is doubtful if the observations recorded are of much

PLATE I.—Retinitis albuminurica ; showing hæmorrhages, œdema about the disc, and bright radiating streaks and spots of degeneration.

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value. The existence of retinal changes, in a pure case of primary lardaceous degeneration, has yet to be placed on record.

Some years ago I collected a hundred cases of contracting kidney from among my out-patients, and these were examined by Mr. Eales, who published the result of his observations in the Birmingham Medical Review for January, 1880. Out of the hundred cases, retinal changes were present in twenty-eight, rather less than the number recorded by Galezowski (fifty out of a hundred and fifty); but decidedly greater than the nine per cent. found by Wagner.

In sixteen of these twenty-eight cases, changes were found in *one* eye only; probably because they are apt to begin in one eye before the other; thus in one case at the first examination no ophthalmoscopic changes were found; two months later several white specks were observed in one eye along a branch of the retinal artery, but there was no evidence of inflammation.

In these sixteen cases the lesions were as follow: In six, several round white patches; in five, one or two spots only; in one, a single recent hæmorrhage near the disc; in two, black specks, associated in one instance with white specks; in one, two large, round, soft-edged, whitish patches close to the disc.

In the twelve cases in which both eyes were affected the following lesions were noted: In four, diffuse retinitis in both eyes; in one, diffuse retinitis in one eye, with a single hæmorrhage in the other; in five, many whitish round patches; in two, a few white patches.

In addition to these twenty-eight cases, there were three in which the disc was abnormal, this structure being abnormally pink (hyperæmic) in one, and abnormally pale (atrophic), with blurred edges, in two. The first was probably a case of incipient neuritis, and the others were very likely atrophy secondary to a slight neuritis; so that if we include them we obtain thirty-one cases out of a hundred, a number very close to the thirty-three per cent. recorded by Galezowski.

Although there is no evidence that these retinal changes ever occur in acute infective nephritis supervening in healthy kidneys, they are very common in connection with the albuminuria of pregnancy. But the albuminuria of pregnancy is preceded and caused by chronic blood poisoning, of which the retinal changes are only another local expression. Doubtless

when the kidneys begin to fail in their function, the blood poisoning rapidly gets worse; but it is a condition which must be dated back some time anterior to the earliest expression of renal trouble.

Pathology.—With the exception of the slight opacity and cloudiness of the retina which may occur in the course of an acute uræmic attack, all these conditions are met with only when the primary disease is of some duration, and the pathological causes at work are at least three in number:—

1. The dyscrasia, or altered condition of the blood.
2. Secondary degenerative changes in the small blood vessels.
3. Excessive pressure of blood within the vessels.

The first is by far the most important, and is probably the starting point of the other two. The dyscrasia is caused by the failure of the kidneys to eliminate the products of disassimilation, and this leads to imperfect nutrition of the tissues, especially to inflammatory and degenerative changes in and around the walls of the small arteries, and also to obstruction to the course of the circulation.

Denissenko denies the existence of an inflammatory exudation, and regards the retinal changes as merely œdematous; in accordance with this view he proposes to substitute the name of ophthalmia Brightica or œdematosa for that of albuminuric retinitis; this opinion appears, however, to be based on a partial view of the facts. Holstoi, who has recently investigated the subject, comes to the conclusion that the affection originates in inflammation of the coats of the smaller arteries, and describes them as having their walls converted into a shining homogeneous mass, recalling the "colloid" change of the vessels of the choroid described by Poncet.

Maguire has expressed the opinion that the lesions are the result of degeneration and not of inflammation; he thinks excessive intravascular tension is the sole cause, and that this alone sufficiently accounts for the hæmorrhages and the nutritive disturbance, but, in view of the positive evidence of inflammatory changes, the explanation is not very satisfactory. Weeks ascribes the alterations to primary vascular changes of a hyaline and fibroid character.

Duke Charles, of Bavaria, describes a general arteritis as the essential lesion in the retinal affections of Bright's disease, the chief changes being in the vascular layer of the choroid and the retina, but more in the former than in the papilla or the

PLATE. II.—Neuro-retinitis albuminurica hæmorrhagica ; showing diffuse exudation, with hæmorrhages in and around the disc.

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retina. The coats of the larger vessels in the retina and papilla present in parts a wavy structure, in other parts they are homogeneous; numerous dissecting aneurysms occur, as well as hæmorrhages into the sheath of the vessel. The inflammatory process is most marked in the capillary area between the small arteries and the veins. He states that the choroidal capillaries possess an actual perivascular sheath, and in some places fibres are present, lying at right angles to the axis of the vessel, between the endothelium and the perithelium. The thickening of the vessels is caused by œdematous swelling of their walls, and by the degeneration of masses of red and white blood corpuscles. In places the lumina are narrowed, and thromboses occur. Near the arteries the capillaries show ampulla-like diverticula and dilatations of their walls. These changes are situated chiefly in the peripapillary zone. He describes an infiltration of the rods and cones by small cells, and the formation of hyaline masses in the granular layer. He found nowhere any trace of sclerosis of nerve fibres. Hæmorrhages occur in the pia-matral sheath of the optic nerve, and its vessels show thickening of their walls. The arteritis is seen also in the vessels of the sclerotic, ciliary body, iris, and conjunctiva.

If we examine a section through a soft-edged white patch we find that the nerve fibre layer is greatly thickened, and contains granular masses formed by the fusiform enlargement of the nerve fibres; these fusiform enlargements often reach a great size, become filled with fatty granules, and ultimately become isolated, so to form spheroidal bodies (*Fig.* 12). Areas may also be infiltrated with a finely fibrillated material, which may be fairly regarded as coagulable lymph. Such an exudation may occur in the outer molecular layer, where large cavities, separated by the remains of the vertical fibres, are filled by this substance. Capillary dilatation, with ampulla-like diverticula of the vascular walls, are also seen in this section.

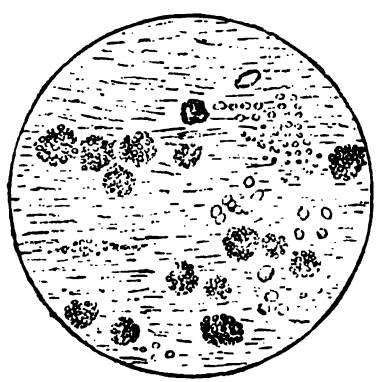

Fig. 12. Section through atrophic retinal patch showing fatty degeneration of exudation. × 250 (after GOWERS).

But in the other form of white patches, so commonly seen radiating from the yellow spot, the lesion is different. Here the round corpuscles and vertical fibres of Müller are affected. The latter become swollen and filled with minute oil globules, and in this condition they possess an undue refractive power, hence their glistening appearance; while the radiated arrangement of the specks is due to the fact that these fibres radiate from the yellow spot.

Diffuse opacity of the retina is mainly due to œdema, the lymph spaces around the ganglion cells of the nerve fibre layer being distended with clear fluid, so that these drop out of the section, leaving large spaces. But there may also be an effusion of coagulable lymph, especially in the outer molecular layer, where it may occupy large cavities separated by the remains of the vertical fibres, or such an exudation may separate the membrana limitans interna and bases of Müller's fibres from the rest of the nerve fibre layer, while the layer of rods and cones may show remarkable thickening. Of less importance are the small grey angular spots of pigment, often arranged in groups, which appear first in the periphery, and are due to changes in the pigment epithelium. I may mention in this place that very rarely choroidal hæmorrhage may occur, giving rise to localised atrophy of this coat and adjacent pigmentary disturbance.

Hæmorrhages occur mainly into the sheaths of the retinal vessels, so that they are usually longitudinal, running in the course of the vessels. Occasionally they may be more diffuse and occupy a large area, or even burst into the vitreous.

Optic papillitis is an interstitial neuritis, with swelling and round cell infiltration of the connective tissue of the nerve, leading in some cases to atrophy of the nerve fibres.

In general retinal periarteritis the inflammation of the arteries is associated with numerous hæmorrhages. Its pathological anatomy has been studied by Ivanoff, who states that the first appreciable change is a serous transudation into the retina, which is for the most part confined to the neighbourhood of the vessels, the inflammation attacking chiefly the outer coat of the arteries, the middle and inner coats remaining comparatively healthy. The outer coat becomes infiltrated with nuclei and delicate fibres, which form an opaque white sheath. This causes thickening of the vessels and encroaches on the lumen, so as to obliterate the smaller ones. By the extension of the inflammation from the sheath of the vessels to the disc, this

becomes swollen. Ivanoff considers the process to be distinct from atheroma on the one hand, or the ordinary arterio-sclerosis of Bright's disease on the other; Wedl believes it to be atheromatous, and Abadie supported this view by pointing out that it only occurs in elderly people, but Nagel has since published a typical example in a young man of 22. The histological details entirely negative the notion of atheroma, which is essentially a disease of the inner coat, while in this condition it is the outer coat which is almost exclusively attacked. Its relationship to Bright's disease is attested by the fact that in five out of the seven hitherto published cases it was so associated.

Among the further changes which occur, apparently by an extension of the same diseased processes, are detachment of the retina, due to effusion taking place behind that membrane, and acute glaucoma from sudden increase of pressure in the posterior ocular chamber. Several cases of this kind have been placed on record by Anderson, Collins, Landesburg, Weeks, and others. Irido-choroiditis has been observed by Leber.

Course of the Lesions.—It is undoubtedly the rule that the more important retinal changes persist until the patient's death; but they may increase or diminish, or even, in some cases, disappear entirely. The last occurs where the renal affection also undergoes considerable improvement or cure, and is most common in the nephritis of pregnancy, which is specially liable to be associated with retinal changes, and yet frequently gets perfectly well, provided that the renewal of the cause is prevented. But, in addition to this qualification of the rule given above, the inflammatory signs, as a rule, diminish and disappear, while the degenerative signs persist. This was shown in the case of a man who was under my care nearly four years ago. He was admitted with loss of sight, headache, and vomiting, but presented all the signs of chronic nephritis, probably due to lead, as he was a house painter by trade. At this time, April 10th, he could read no type at all, there was intense papillitis in the left eye, with a moderate degree of the same lesion on the right side, and characteristic radiating patches around both yellow spots. Under appropriate treatment his general condition improved, his headache disappeared, and his vision returned so far that he was able to read a book or newspaper. On May 20th his vision was tested R = $\frac{6}{9}$ L = $\frac{6}{10}$. The state of the fundus was

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noted on May 30th, when the inflammation of the discs had subsided, although the peri-macular patches were still present, and had even undergone some increase in number.

In 1881 Mr. Eales and I had under observation a young woman, aged 19. She was at that time suffering from dimness of vision, and the ophthalmoscope showed slight swelling of both discs, with white, soft-edged patches around both disc and macula, but no radiating, bright streaks. The urine was albuminous, and contained casts. She improved under treatment and, in spite of a relapse, two years later her fundi were normal, and her V = $\frac{15}{xx}$ in both eyes. We managed to find her again in 1888, and got her to come to see us, when we had the satisfaction of finding that her general health was fairly good, her urine was still albuminous, but contained no casts, and, what is most to our present purpose, her fundi were quite normal, with the exception of a small pigmented spot in each retina, with slight disturbance of the choroidal epithelium. A case ending in recovery in a male has also been published by Adamück, while Novelli has related one of the not uncommon cases of recovery from puerperal retinitis. It must therefore be admitted that the soft-edged patches may disappear and heal. Hæmorrhages undoubtedly become absorbed in course of time. Dr. Miles Miley has mentioned the case of a man, aged 48, under the care of Dr. Stephen Mackenzie, who, on July 2nd, 1885, was stated to have hæmorrhage and white patches in both eyes, and on October 17th, 24th, and 30th to have no changes present. Diffuse neuro-retinitis subsides, but always leaves more or less permanent damage behind; and even the radiating streaks themselves may disappear where the renal disease undergoes marked improvement. The course of multiple periarteritis is probably always progressive.

Diagnostic value.—The diagnostic value of these changes is not equal and has marked limitations. For example, hæmorrhages occur pretty commonly in blood diseases, such as leucocythæmia, pernicious anæmia and purpura, while Mr. Eales has described a number of cases in young lads without any constant etiological factors, except their age and constipation. These hæmorrhages are as a rule rounded and irregular, but they may be striated and longitudinal like those of Bright's disease. I have seen a case of chlorotic anæmia, who brought with her a note signed by a very competent ophthalmic surgeon to say that the bearer had typical

albuminuric retinitis, the fundus presenting numerous soft-edged white patches. Moreover, Dr. Edmunds has recorded a case of cerebral tumour where, in addition to intense optic neuritis, there was a group of radiating patches around the macula which appeared absolutely characteristic of albuminuric retinitis. It is also certain that diffuse neuro-retinitis occurs in cerebral tumour and in Bright's disease in a form which is indistinguishable. Brudenell Carter has related a case of diffuse retinitis which was regarded as one due to brain disease by Dr. Hughlings Jackson, Dr. Noyes of New York, and by several members of the Ophthalmological Congress then assembled in London. The boy died of pleurisy supervening upon advanced kidney disease, and no trace of brain mischief could be found on most careful examination. Nearly at the same time there was in hospital a young woman whose eyes presented typical examples of the changes often associated with albuminuria, but in whom, after death, a tumour was found in the cerebellum, while the kidneys were perfectly healthy. Lastly, multiple retinal periarteritis, though generally associated with Bright's disease, is met with apart from this condition. We must therefore admit that none of these appearances is absolutely pathognomonic; and it is certain that a diagnosis based solely upon the appearance of the fundus oculi is fallacious. Ophthalmic surgeons are well aware of this, and always look for some of the more obvious signs of Bright's disease to confirm the ophthalmoscopic appearances. But while we cannot allow them the proud position of being all-sufficient for diagnosis, we must assign them a very high place among those indications of disease which, taken together, lead to an indisputable conclusion. Moreover, their diagnostic value in practice is all the greater because it not uncommonly happens that failure of sight is the first symptom of deranged health observed by the patient, so that the practitioner who is consulted for an apparently trifling impairment of vision must be able to recognise the grave condition of the patient.

Among the minor phenomena observed in the *fundus oculi* of Bright's disease are pallor of the vessels with great sharpness of their central light streaks; often where such vessels cross a vein they may be observed to obstruct its circulation, and such a vein is peculiarly likely to be the source of hæmorrhages (MARCUS GUNN).

Narrowing of the arteries may be seen associated with

dilatation of the veins. Gowers believes in a persistent spasm of the arteries, but this narrowing is constantly seen as a consequence of retinal disease apart from Bright's disease.

In reference to this question Mr. Eales says, "I cannot confirm the statement of Dr. Gowers, that this (arterial contraction) is common. Only twice, I think, some slight contraction existed, but I did not feel sure that it was abnormal even in these cases.

"I have recently had a case of diffuse hæmorrhage into the retina; the hæmorrhages have cleared; the retina looks quite healthy, but vision is imperfect, and the arteries have contracted very much since I first saw the case. Here, though no sign of disease is visible, I think we may safely infer that the retina is damaged, and that the contraction is a consequence of degeneration in the retina, as it was not noticeable in the early stage of this case, and contraction of the retinal arteries from this cause is common."

Choroidal hæmorrhage may occur leading to circumscribed atrophy and pigmentary disturbance.

"Colloid" degeneration of the vessels of the choroid has been described by Poncet.

After parenchymatous retinitis there may be some pigmentary degeneration of the choroid in the form of small grey spots arranged in groups (GOWERS).

Thickening of the adventitia or lymph sheath is very common, but always in association with retinal disease.

Embolism of the retinal arteries has been described, but of late years it has come to be recognised that plugging of these vessels is more usually thrombotic, and it is probable that such statements should be taken to imply that the artery was blocked by a clot, which blocking, in accordance with the prevalent doctrines of that time, was assumed to have come from a distance and not to have been formed *in situ*, although this last supposition is now recognised to be the more probable explanation.

Hæmorrhage into the vitreous may occur from the bursting of a large retinal extravasation. It causes permanent damage to vision, and may give rise to glaucoma (GOWERS).

Effects on vision.—In the great majority of cases presenting retinal change, that is, in those in which only a few degenerative specks or hæmorrhages are found, vision is unaffected. Acute neuro-retinitis may be present without causing any complaint from the patient, but this is exceptional. As a rule vision is

affected in proportion to the extent of the disease, but these patients rarely become quite blind, generally retaining perception of light sufficient to enable them to see to get about.

Prognostic value.—Valuable as are these signs for the purposes of diagnosis, the information derived from them for prognostic purposes is of a more precise and definite kind, though even here no absolute rule can be established. Putting the matter generally we may say that serious retinal changes indicate advanced disease and the approach of death, the great exception to this rule being puerperal nephritis, which generally recovers if pregnancy does not recur. To be more precise, we may define serious retinal disease as either diffuse neuro-retinitis or well-marked patches of degeneration around the yellow spot. A few white specks are of no definite significance, they may be found in advanced cases, but Mr. Eales observed them in lads with functional albuminuria under my care. By functional albuminuria, I mean albuminuria occurring in persons who show no other sign or symptom of renal disease, and who an experience of many years now enables me to say do not develop any such condition. The soft-edged rounded patches are also to be regarded as not inconsistent with a moderately hopeful view of the case, if other symptoms warrant it. Hæmorrhages are less favourable than either of the last two, but their value for prognosis depends upon the kind of case in which they occur. That is to say, if they occur in chronic Bright's disease they should be regarded as indicating wide-spread arterial changes, which may prove dangerous to life in various ways, but apart from these conditions, they do not diminish the prospects of life. I am not in a position to state anything definitely as to the significance of multiple peri-arteritis, but the case recorded by Dr. Mules has since died, and from the nature of the lesion I should be disposed to class it with the gravest forms of retinal disease, and therefore of the worst prognostic meaning.

Dr. Miles Miley has, perhaps, made the most important contribution to the statistical side of the general question. He has collected 164 cases of chronic renal disease at the London Hospital, out of which number 51 were definitely stated to have had their eyes affected. Of the remaining 113, there died in hospital 28, or 23 per cent.; while of the 51, there died during the same period 27, or nearly 53 per cent. The mortality of the affected cases was therefore more than double that of the unaffected. But means were taken to trace the

remainder of the 51 cases, and 18 more were proved to be dead; the remainder could not be accounted for. Of those that died, one lived eighteen months, but all the others died within a year. But it must be borne in mind that all these cases were sufficiently advanced to have required treatment as in-patients at the hospital, so that the extremely rapid termination of the greater number must be attributed to the grave nature of the general constitutional condition of the whole group of cases. Had they been selected from an out-patient clinic, I have no doubt the average duration of life would have been longer. Still, I think we are not justified in expecting that a patient who is suffering from chronic non-puerperal nephritis, who has diffuse retinitis, or well-marked degeneration around the yellow spot, will live long, and I should be disposed to place the extreme duration of life under such circumstances at two years, whatever the state of the general health might be. Dr. Collins thinks detachment of the retina in retinitis is a very bad prognostic sign; and this is probably worth bearing in mind. as the occurrence of this complication marks an extreme degree of tissue degeneration. He is also of opinion that those with merely fatty degeneration, by which I take him to mean soft-edged patches, or hæmorrhages, are the most favourable. Here, again, I am disposed to agree with him, and I have already expressed myself in this sense.

Let us now try to sum up the facts and conclusions of this lecture. We have seen that the retinal affections in Bright's disease vary very much in their ophthalmoscopic appearances, their anatomical nature, and in their diagnostic and prognostic value. We have learnt that they are probably all dependent upon a dyscrasia which causes effusion of serum or blood, inflammation of the vascular walls or of the nervous tissues, and secondary degenerative changes. Further, it has been abundantly proved that none of these changes, taken singly or together, justifies the diagnosis of Bright's disease, but that they may often be the first indication of the disease, which is easily confirmed by the usual examination of the urine, pulse, etc.; and we may lay stress upon the imprudence of neglecting to look for these confirmatory signs before committing ourselves to an opinion upon the nature of any case. Finally, we find that, for prognostic purposes, these signs may be roughly divided into two classes: (1,) The grave—which includes diffuse neuro-retinitis, radiating patches around the yellow spot, and multiple

periarteritis; (2,) The benign—including simple œdema, hæmorrhage, and soft-edged round patches; and we may venture to lay down the rule that, apart from puerperal nephritis, the subjects of the former class will not live long, almost certainly not more than two years; we should also be distrustful of hæmorrhages, if they occur in persons whose condition is otherwise unfavourable. I do not think we can ever regard any retinal change as favourable. The above classification is only intended to separate those changes which justify, even in the absence of other indications, a very grave judgment of the future from those which do not afford grounds for taking a more gloomy view of the case than may be warranted by its other features.

Possibilities of Cure.—Though all authorities admit the possibility of cure and the disappearance of spots, and instances of marked improvement have been already related, such recoveries are rare. This is due, not to any essential incurability in the retinal condition, but to its dependence upon an incurable renal disease in its last stages.

Summary. 1.—The retinal changes of Bright's disease consist of neuritis and neuro-retinitis, periarteritis, hæmorrhages and white patches of degeneration.

2.—These do not possess any specific characters which enable the observer to diagnose Bright's disease with absolute certainty from them alone.

3.—They are dependent chiefly upon the disordered state of the blood, with which, in the case of hæmorrhages, the high arterial tension and the diseased vascular walls co-operate.

4.—They may be divided for prognostic purposes into two classes: (1,) The grave—including diffuse neuro-retinitis, radiating patches around the yellow spot, and multiple periarteritis; (2,) The benign—including simple œdema, hæmorrhages and soft-edged rounded patches; the subjects of the former group, with the exception of cases arising from pregnancy, do not as a rule live more than two years; of the latter group, it can only be said that their presence does not make the prognosis of the case better or worse; the apparent exception of the albuminuria of pregnancy is explained by their being due, in that case, to a dyscrasia not dependent solely upon the renal disease.

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CHAPTER IX.

HISTORY—CLASSIFICATION—ETIOLOGY.

ALTHOUGH Van Helmont regarded the kidneys as the seat of the causation of dropsy, and the discovery of Cotunnius that the urine of dropsy was coagulable by heat was published as early as 1770, there can be no doubt that the whole honour of establishing the true relations of dropsy and albuminuria to disease of the kidneys belongs to the great physician and pathologist of Guy's Hospital, RICHARD BRIGHT.

Blackall, of Exeter, would perhaps have forestalled him had he enjoyed equal opportunities for making *post mortem* examinations; but, in the fourth edition of his book, published in 1825, Blackall shows himself to be entirely ignorant of the local causes of dropsy, assigning to it a constitutional origin, and inclining to the opinion that albuminuria was due to *the elimination of the dropsical fluid by the urinary passages.*

Bright's *Reports of Medical Cases*, published in 1827, present a striking contrast to this vague humoralism by the definite solidism of his pathology. He distinctly ascribes albuminuria and dropsy to the altered anatomical condition of the kidneys, and he figures accurately the changes in the kidneys just as they are recognised by us to-day.

In his papers in the first volume of *Guy's Hospital Reports*, published in 1836, Bright added a great deal of clinical and pathological information.

He had learnt that dropsy might be slight or altogether absent, and that albuminuria might require looking for. He described the various complications, the inflammations of serous membranes, hæmorrhages, apoplexies, convulsions, blindness, and coma; he drew attention to the frequency of cardiac hypertrophy, and suggested an explanation which still holds its ground.

He recognised the importance of alcohol and exposure to cold as etiological factors, while his views on prognosis were truer and more liberal than those which afterwards became current.

But on the actual nature of the pathological process his ideas were cramped by the contemporary state of pathological doctrines. Just as in these days every disease is ascribed to a *microbe*, in Bright's time everything was regarded as due to a *deposit*. Laennec called tubercle and cirrhosis of the liver deposits. So Bright thought the various anatomical types of Bright's disease were stages in the evolution of a deposited material, and the hard granular kidney was the ultimate result of the process.

Rayer, in 1839, correctly described the inflammatory nature of the lesion, and some years after (1851) Frerichs explained the different anatomical types by his doctrine of three stages: (1,) Hyperæmia with exudation; (2,) Fatty degeneration of the exudation; and (3,) Absorption of the exudate with atrophy of the organ.

Johnson, in his "Diseases of the Kidney," published in 1852, made two important additions to the subject: (1,) He showed that the chief seat of acute inflammation was the tubules, and that in the sequel the tubular epithelium underwent necrosis, desquamation, and fatty degeneration; (2,) He differentiated the small red kidney as a type which occurs independently of acute inflammation.

In 1858 Virchow gave an academical form to these discoveries by describing three conditions: (1,) Parenchymatous inflammation, originating in the tubular epithelium; (2), Interstitial inflammation, originating in the connective tissue; and (3,) Amyloid degeneration, originating in the blood vessels.

Amyloid, waxy or lardaceous degeneration had been previously recognised by Rokitansky and Johnson, but only as a complication, not as a distinct type.

Rosenstein, in 1860, found Virchow's academic classification too rigid, and described: (1,) Hyperæmia; (2,) Catarrhal nephritis; (3,) Diffuse nephritis; and (4,) Amyloid degeneration.

Grainger Stewart, in 1868, recognised three forms of Bright's disease: (1,) Inflammatory, having three stages: (*a*,) Of inflammation; (*b*,) Of fatty transformation; (*c*,) Of atrophy. (2,) Waxy or amyloid, also having three stages: (*a*,) Affecting vessels only; (*b*,) Transudation into tubules; (*c*,) Atrophy. (3,) Cirrhotic or contracting.

In 1872 Gull and Sutton introduced an entirely new doctrine to explain the pathogenesis of the contracting kidney.

They re-discovered the thickening of the vessels which had been described by Johnson, and announced the existence of a generalised affection of the small arteries and capillaries, to which they gave the name of *arterio-capillary fibrosis*, and of which they maintained the kidney lesion was merely a pronounced local expression; the vascular degeneration having led to atrophy of the surrounding tissues.

But the doctrine of interstitial nephritis received a new impetus from the careful work of Kelsch, published in 1874, and in succeeding years it was endorsed by Bartels, Charcot, and Grainger Stewart.

It had never been accepted by Johnson, Moxon or Roberts in this country, or by Rosenstein, who declared "That there could not properly be said to be either strictly parenchymatous or strictly interstitial nephritis," both tissues being affected, and "that large white and small red kidneys were alike the result of *diffuse* inflammation."

Weigert gave great support to this opposition by a paper published in 1879, in which he maintained that the parenchyma and the stroma are affected in all cases of chronic Bright's disease, and that pure parenchymatous nephritis exists only as an acute disease. These views met with the concurrence of Bamberger, and were supported by the experiments of Gräwitz and Israel, who found that artificially induced nephritis was followed indifferently by the small red or large white kidney.

In 1880 I expressed the results of my own histological observations in the following words: "The small red and large white kidney, and all the intermediate varieties, are the result of inflammation which affects all the tissues, but varies very greatly in intensity. The parenchyma being the most highly organised tissue, suffers most in proportion to the intensity of the inflammation. The large pale kidney is the result of prolonged or repeated severe inflammation; on the other hand, the small red kidney indicates an inflammatory process of prolonged duration but of minimum intensity; and the intermediate varieties correspond to all the different degrees of intensity possible between the two extremes. The fact of the existence of *an indefinite number of intermediate or mixed forms* between the two typical varieties of the large white and small red kidney is a strong argument in favour of the doctrine of unity."

Since that time there has been no conspicuous attempt to

revive the doctrines of Virchow, and the opinion that the lesion is a diffuse nephritis in all forms of chronic Bright's disease has steadily gained ground.

CLASSIFICATION.

In the preceding sketch of the history of the doctrine of Bright's disease, I have recorded the failure of successive attempts to classify the various clinical forms upon an anatomical basis.

I propose to adopt an etiological classification, which I hope will be found to adapt itself to the facts of clinical observation as well as to pathology. The following are the proposed divisions:

(1,) Infective Nephritis;
(2,) Toxic Nephritis;
(3,) Obstructive Nephritis.

The first division includes all those cases of acute or chronic nephritis occurring as a result of acute or chronic infective diseases. The nephritis is directly dependent upon the infective process, hence its name. Anatomically it includes most cases of acute parenchymatous nephritis, of chronic fatty kidney, and many of typical granular kidney, for numerous observations have proved that acute nephritis following infective disease (*e.g.*, scarlatina, enteric fever, pneumonia), may develop this form.

The second division includes the great group of chronic Bright's disease due to lithæmia, and is specially associated with the small red granular kidney, but owing to the occurrence of intercurrent acute and subacute attacks of nephritis the kidneys are often enlarged and fatty. It probably depends upon irritation of the kidneys by the excessive elimination of poisons of which uric acid is the type. It includes the acute nephritis of acute gout, of poisoning by animal, vegetable or mineral poisons, and certain cases of primary acute nephritis usually attributed to chill, but in which there is probably an already existing dyscrasia. Such acute cases are met with occasionally in individuals who get drunk on beer and lie out all night.

The third division includes all cases dependent upon obstruction to the outflow of urine. They occur commonly in males as a consequence of stricture or enlarged prostate, in females from pressure on the ureters caused by pregnancy or pelvic diseases.

In each of these classes we may meet with the urinary and other symptoms of acute or chronic nephritis, while the *post mortem* appearances may be those of acute nephritis, of chronic fatty kidney, or of contracting kidney.

Lardaceous or *waxy* degeneration is not made a special group because it is only when associated with chronic nephritis that it deserves to be called Bright's disease. General lardaceous degeneration affecting liver, spleen, kidneys, intestinal mucous membrane, lymphatic glands, heart, etc., has no other title to be called Bright's disease than the occurrence of albuminuria, and even that is not always constant (FÜRBRINGER). Whatever may have been the case twenty years ago, it cannot be maintained now, and certainly will not be admitted here, that albuminuria and Bright's disease are synonymous.

The lardaceous kidney of most authors is chronic nephritis as it occurs in chronic infective diseases, *e.g.*, long standing suppurations, phthisis, etc., in which lardaceous degeneration may occur just as it may in any other form of chronic Bright's disease.

Its relation to suppuration is by no means so constant as has been taught; for out of sixteen cases of chronic nephritis occurring in these circumstances, collected from the pathological registers of the General Hospital, lardaceous degeneration was present in two only.

I admit that lardaceous disease is less common in Birmingham than in London or Edinburgh; this is a striking and curious fact; but the disease is by no means unknown, and its relative rarity makes its true relation to Bright's disease more apparent.

This is after all only reverting to the older opinion of Rokitansky and Johnson.

GENERAL ETIOLOGY.

PREDISPOSING CAUSES.—There can be no doubt in the minds of pathologists of the remarkable frequency of Bright's disease in this country, although the Registrar-General's returns and even our hospital registers fail to give an adequate account of it.

Out of a total number of deaths in England and Wales for the year 1884, amounting to 530,828, only 6,297, or 1·1 per cent., are returned as having been registered under the various terms which are included by Bright's disease. In this district,

the West Midland, there were only six hundred and ninety out of a total of 56,938 deaths, or 1·2 per cent.

In London alone during that year there were 11,000 deaths in persons over fifty years of age, of which only seven hundred and sixty were registered as Bright's disease; but Mahomed has told us that in the *post mortem* registers of Guy's Hospital, he found out of a hundred and fifty cases over fifty years of age, sixty-two instances of chronic Bright's disease, a proportion of one in 2·42, so that instead of seven hundred and sixty, there should have been 4,546 cases of Bright's disease.

On examining the pathological registers of the General Hospital for ten years, from 1875 to 1884, out of 1,213 deaths at all ages there were no less than three hundred and eighty-three cases of acute and chronic Bright's disease, giving a percentage of 31·5 or a proportion of about one in three.

But the Registrar-General's returns show that there has been an increase in the number of cases registered as due to this cause, the increase being mainly in the less obvious form of chronic Bright's disease; for while in 1875, out of a population of twenty-two millions, 3,841 cases were registered under Bright's disease, of which number nine hundred and seventy-eight were described as "*nephritis*"; in 1893, with a population of twenty-nine millions, 8,098 cases were registered as Bright's disease, of which number only 1,912 were described as "*acute nephritis*." The increase of population was thirty-one per cent., of cases of *nephritis* sixty-two per cent., and of Bright's disease one hundred and ten per cent.!

This result is in all probability due to the fact that the profession is beginning to look for latent cases of Bright's disease and has learnt to recognise them better than was formerly the case.

I think we may assume the power of recognition to be a uniform factor in the comparison of one registration district with another, for the purpose of ascertaining whether there is any great difference in the frequency of the disease in particular portions of this kingdom. The following are the results of the figures worked out as percentages for the year 1884:—

All England	1·1 per cent.
London	1·4 „
South Eastern	1·4 „
South Midland	1·4 „
Eastern	0·9 „

South Western	1·4 per cent.
West Midland	1·2 „
North Midland	1·0 „
North Western	1·0 „
York	1·0 „
Northern	0·7 „
Wales	1·4 „

This district, the West Midland, is very little above the average. The influence of great towns does not seem to be very decided, looking at the high figure of Wales, and the low figures of all the northern districts.

I am not inclined to regard this table as giving information of a too trustworthy character. It is very remarkable that the eastern district, in which stone is so common, stands so low. It is contrary to what we know of the etiology of Bright's disease, and is probably explained by the fact that the form of the disease set up by uric acid is the type most likely to be overlooked.

Purdy finds that Bright's disease is very much more common in the Eastern and Northern parts of the United States; it is most common in New Jersey, New York, Connecticut, Massachusetts and New Hampshire, least prevalent in Georgia, Nebraska, North Carolina and Arkansas. His figures of the mortality in the various regions are very striking:—

Eastern States	19·73 per million.
Northern States	17·38 „
Southern and Western States	1·5 to 2 „

The prevalence of Bright's disease is said to be equally great in Holland, Denmark, Scandinavia, and on the shores of the Baltic, which share the common predisposing cause, a COLD MOIST CLIMATE.

In such an atmospheric medium the functions of the skin are habitually depressed, and an undue share of the work of elimination is thrown upon the kidneys. A general pathological law links together excessive function and proneness to disease. In tropical climates we have a converse illustration in the great prevalence of skin diseases.

But, in all probability, it is not simply an excess of work that the kidneys are called upon to do. Garrod states that suppression of perspiration is followed by increased acidity of the urine, and from this we may infer diminished alkalinity of the blood, leading to the accumulation of uric acid in the system.

Semmola believed the chief effect of chill to be an alteration of the blood albuminoids resulting in renal irrita-

tion, hyperæmia and albuminuria, which is followed by general nutritive changes and anatomical alterations in the kidneys. In effect he thought that the altered blood albuminoids act like egg albumen when injected into the veins, becoming readily diffusible through the glomerular walls and appearing in the urine. Thus he made albuminuria the first link in the chain of sequences, to be followed by structural alteration in the kidney.

Such a theory needs proof, and of this none is offered.

On the contrary, the analogy of egg-albuminuria is a weak one, for it leaves no ill effects on the kidneys (SNYERS). Moreover, Tizzoni found that albumen from the urine of Bright's disease when injected into the veins of animals did not cause albuminuria, and there are many cases on record or known to me of albuminuria that has persisted for years without giving rise to any other symptom of Bright's disease.

Sex.—It is commonly stated that Bright's disease is more common in males than in females. The pathological register of the General Hospital shows its proportion to all deaths in either sex to be in males 43·4, in females 40·6. Bamberger finds no difference.

In women there are special causes, such as pregnancy, uterine and ovarian tumours, and pelvic inflammation, which are important and common factors; but against these we may place the greater exposure of men, their habits in food and drink, and the frequency of cystitis, stricture, etc.

Age.—Acute Bright's disease is much more common in children than adults on account of its relation to acute infective diseases, especially scarlatina. Chronic Bright's disease is more frequent after middle life.

The mortality from Bright's disease shows a progressive increase as age advances; a fact permitting the just inference that chronic Bright's disease is much more fatal than acute.

	Under 5	5 to 15	15 to 25	25 to 35	35 to 45	45 to 55	55 to 65	65 to 75
Males	168	145	189	290	469	644	724	606
Females	140	123	174	284	412	482	543	488

Heredity.—There is an undoubted tendency in Bright's disease to attack members of the same family and to appear in successive generations.

In a case of contracting kidney in a lad, seen in consultation with Dr. J. A. Lycett, of Wolverhampton, his father and two paternal uncles had died of Bright's disease. Other striking instances have been published (MEIGS, KIDD). This may be attributed to its relation to gout and lithæmia. There is probably an inherited vice of structure or function; a thin ill-developed skin is undoubtedly a transmissible peculiarity which has come under my observation in this connection. The habit of constipation, upon whatever it depends, is also a feature common to families, as are also the habits of eating and drinking to excess. The following is an example of three cases of Bright's disease in one family.

CASE 3.*—William E., aged seventeen, waggoner, admitted Dec. 11th, 1887, with dropsy of face, legs and abdomen. Four weeks before he had got very wet; this was followed by shivering, lumbar pain, swelling of face, legs and belly, with diminished urine. In a week the pain went away, the urine increased in amount, and the dropsy diminished.

He could remember no previous illness, and his statement was confirmed by his mother; he had never had scarlatina. His work exposed him to wet and cold.

His father had died of kidney disease, aged thirty-two; and an uncle was at present under treatment in hospital for the same condition.

Patient was a slightly-built lad, with a little œdematous swelling of face and legs. T. 99·2°; P. 72; R. 19; tongue clean; bowels regular; no ascites; liver and spleen normal.

Heart's apex in fifth interspace internal to vertical nipple line; a systolic murmur at apex. Pulse 72, regular, full. Urine 48 oz.; sp. gr. 1010; acid; contains albumen and blood.

Dec. 14th. Better; no œdema of legs; urine 60 oz.

Dec. 15th. Urine 50 oz.; sp. gr. 1018; acid; pale straw colour; mucous cloud; urea 242 grains *pro die*; albumen a cloud; a trace of blood; hyaline, epithelial and granular casts, red and white blood corpuscles and renal epithelium.

Dec. 16th. No œdema of face now.

Dec. 26th. Urine 52 oz.; sp. gr. 1014; acid; opaque, pale straw colour; mucous deposit; urea 251·68; a cloud of albumen; a few granular casts, red and white blood corpuscles and a few renal epithelia.

Jan. 4th. Allowed to get up.

Jan. 5th. Urine 46 oz.; sp. gr. 1020; acid; dark straw colour; mucous deposit; urea 344 grains *pro die*; a cloud of albumen; a very little blood; no casts or renal epithelium.

Jan. 10th. Abundant hæmaturia, causing headache; sent back to bed. No œdema.

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* Recorded by Mr. Teichelmann, clinical assistant.

Jan. 14th. Urine 52 oz.; sp. gr. 1015; neutral; pale straw colour; urea 274 grains *pro die*; a faint cloud of albumen; no blood; a few hyaline casts.

He was discharged on Jan. 25th, without any further relapse.

Social State.—Bright's disease attacks all classes, but there are occupations that are specially liable to it; these are, the manufacture and sale of alcoholic drinks, brewers, distillers, publicans, and the like; workers in lead, file casters, glass cutters, workpeople in white lead factories, painters, lapidaries, etc.; those specially exposed to cold or damp—well sinkers, miners, etc., and to extreme changes of temperature—furnace men, iron workers, stokers, etc.

Diet.—Our habits as to food and drink constitute an etiological factor of great importance.

We are great eaters of butcher's meat, which is not only the great source of urea and uric acid, but also contains a large quantity of acid salts, by which the alkalinity of the blood is reduced with results already detailed.

We aggravate this evil by drinking beer, containing a large amount of acid, chiefly in the form of acetic acid.

Finally, we consume an enormous quantity of alcohol in other forms, which is almost wholly eliminated by the kidneys, and which certainly leads to structural disease of the liver.

Glaser examined the urine of a number of healthy young men before and after taking alcohol, and found that the after urine contained leucocytes, tube casts, and large quantities of crystals of oxalate of lime and uric acid. The effect of a single dose passed off in thirty-six hours but continued excess produced a cumulative effect.

Previous Diseases.—Chronic heart, lung, and liver diseases, by leading to impairment of assimilation, and especially to the imperfect fulfilment of the great urea-forming function, are undoubtedly remote causes of Bright's disease.

So, too, habitual constipation predisposes by favouring a dyscrasia caused by imperfect intestinal elimination, as well as perhaps by the absorption of animal alkaloids, formed in the putrefactive processes which take place when food remains too long in the alimentary canal.

EXCITING CAUSES.—Of the *exciting causes* of Bright's disease, there are three great groups, whose efficiency is established by an overwhelming mass of evidence. The best known of these clinically is the great group of *acute* and *chronic infective diseases.*

Acute diseases, such as scarlatina, pneumonia, typhoid fever, variola, diphtheria, measles, varicella, tonsillitis, vaccinia (PERL), cholera nostras and Asiatica, and acute rheumatism (E. WAGNER), give rise to acute nephritis; while chronic diseases, such as phthisis, chronic septicæmia, and malarial fever cause chronic nephritis.

Is there any primary acute infective nephritis which occurs apart from the poisons of these diseases? Of late years a series of cases supporting this view has been published by Fiessinger, Mannaberg, Letzerich, Black-Milne, and others, which cannot be overlooked. Fiessinger describes an epidemic of nephritis in the little town of Oyannax in the department of Ain, where there was no evidence of direct transmission, and no concurrent epidemic or fever was present. Mannaberg and Letzerich both isolated organisms which set up nephritis in animals.

Gaucher attributes the nephritis to the irritation caused by the increase of extractives (kreatin, kreatinin, leucin, tyrosin, xanthin, and hypoxanthin) in the blood which are eliminated by the kidneys, and which he has proved by experiments on animals can set up nephritis. This suggestion links this with the next great group, that of *poisons*.

The most interesting and important of these are those substances which are formed in the body, and of which we may take *uric acid* as the type (MURCHISON). They are normal products of disassimilation, but under certain circumstances are produced in excess. These circumstances have been already alluded to. They are circumstances of climate, of individual conformation, of occupation, and above all, of habits as to food and drink; also the presence of pre-existing diseases, especially of the heart and liver. Poisoning of this kind is usually a very chronic and insidious process, often giving rise to no symptoms until the destruction of the kidneys has advanced so far that the dyscrasia, which hitherto has been only the *cause* of the renal disease, now becomes intensified by the failure of the kidneys to eliminate the impurities from the blood, and sets up all the constitutional disturbances known as uræmia. In other cases the disease is discovered earlier, before the kidneys are so far destroyed, when the destructive process may be checked by treatment designed to limit this auto-intoxication.

Many other poisons are known to be efficient causes of

nephritis, but are not of great clinical importance. The following is a list of them :—

Animal Poisons :—Cantharides

Vegetable Poisons :—Oxalic acid
Opium (NAUWERCK)

Mineral Poisons :—Arsenic
Mercury
Iron
Manganese
Cobalt
Nickel
Zinc
Lead
Sulphuric Acid
Nitric Acid
Hydrochloric Acid
Carbolic Acid
Ammonia
Iodoform

The third group comprises all *obstructive causes* from pressure on or diseases in the urinary passages. In males the principal conditions are stricture, enlarged prostate, and tumours and diseases of the bladder, *e.g.*, cystitis, calculus ; in females pregnancy, uterine and ovarian tumours, pelvic inflammations, and bladder diseases.

Simple obstruction sets up a chronic inflammatory process tending to contraction of the kidney. Kidneys which are undergoing this process of obstructive atrophy are very liable to attacks *of acute interstitial inflammation* originating in the medulla and spreading to the cortex. Such attacks may be set up by *cystitis*, or by even a slight traumatism such as the *passage of a catheter* for the first time.

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CHAPTER X.

INFECTIVE NEPHRITIS.

THIS division includes all cases of acute nephritis where the inflammation is set up by an acute infective disease. It also includes all those cases of chronic nephritis occurring as the direct result of chronic infective processes as in phthisis, prolonged suppurations, etc., and also those occurring as a sequel to acute nephritis of infective origin.

ETIOLOGY.—The following infective diseases are known to cause acute nephritis: Scarlatina, diphtheria, pneumonia, enteric fever, exanthematic typhus, remittent fever, malarial fever, variola, measles, varicella, vaccinia, cholera nostras and asiatica, cholera infantum, infantile diarrhœa, suppurative meningitis, acute myelitis, whooping cough, mumps, acute rheumatism, tonsillitis, erythema nodosum, erysipelas, septicæmia, ulcerative endocarditis, cancrum oris, and anthrax. In the greater number of cases the disease is not recognised at the time.

Phthisis, tubercular diseases of bones and joints, malaria, syphilis, and chronic septicæmia, set up chronic nephritis.

The disease is directly due to the infective process, and probably depends upon the irritation of the kidneys during the elimination of toxins.

Specific micro-organisms have been found in the kidneys in cases of diphtheria, pneumonia, septicæmia, and ulcerative endocarditis, but as they are only exceptionally present, it is reasonable to conclude that they are not essential to the production of the nephritis; they are found in the kidney because they exist in the blood, and it is the natural channel for their elimination.

That nephritis has been caused experimentally by the injection of micro-organisms (micrococcus pyocyaneus, CHARRIN and BOUCHARD) proves that this organism may set up an acute infective process in which the kidney suffers, for as Bluhm puts it, any infection may give rise to Bright's disease, even although it is slight and abortive.

The same explanation may be given of some of the cases of so-called *mycotic* nephritis described by Litten, Bamberger, Aufrecht, and Mircoli, but there is a steady accumulation of evidence pointing in the direction of the occurrence of *primary acute nephritis*, as the result of the agency of perhaps several species of micro-organisms which attack the kidneys themselves, just as the pneumococcus attacks the lung.

Non-specific micro-organisms have been frequently found in the nephritis of acute diseases, *e.g.*, variola, scarlatina, and cancrum oris, but they have no pretension to any special etiological significance.

ACUTE INFECTIVE NEPHRITIS.

MORBID ANATOMY.—In the majority of cases during the first week the kidneys undergo no change in size, shape, or colour.

After a week, if the disease persists, the kidneys become more or less enlarged, pale in colour, or mottled red and white. On section, the swelling and pallor or mottling are seen to be in the cortex, the outspread pyramids retaining their red colour.

Histology.—The following is a brief summary of the changes in acute nephritis (under six weeks) with a magnifying power of 450 diameters :—

Blood vessels.—The blood vessels are nearly always full of blood clots, especially below the capsule and in the medulla. They are sometimes greatly dilated. Occasionally thrombi formed of leucocytes are seen in the vessels of the cortex.

Glomeruli.—The capillaries are often full of clots; the endothelial nuclei on the tuft are always distinct and often increased in number. Sometimes the capsular space contains blood clot, at others there is some local accumulation of cells from inflammatory exudation.

Fig. 12. Convoluted tubule in acute nephritis. The epithelium is cloudy, swollen and ruptured.

Tubules.—The epithelium of the convoluted tubes and Henle's loops is generally vacuolating (*Fig.* 13), that is, undergoing a process of atrophy by shedding its protoplasm, leaving only the basal part with the nuclei.

The cavity of the tubules becomes filled with spherical droplets and granular matter derived from the epithelium (*Fig.* 14). In some cases the epithelium appears to be undergoing simple necrosis, breaking down into granular material. The epithelium of the collecting tubes appears to undergo no pathological change, but the cavities of many tubes are filled with droplets and granular matter forming casts.

Fig. 14. Convoluted tubule in a cute nephritis. Epithelium granular, partially destroyed, only the basal portion remaining. The lumen of the tubule is filled with protoplasmic droplets and granular matter.

Stroma. — In scarlatinal nephritis the stroma of the cortex and medulla is swollen and often filled with round cells. In other forms there are only a few round cells, and in the majority of cases it is only slightly swollen and hyaline.

This description shows the affection to be mainly an acute catarrhal inflammation affecting the epithelium of the convoluted tubes. In scarlatinal kidneys, interstitial and glomerular affections are often pronounced.

SYMPTOMS AND COURSE.—As a rule patients with acute nephritis are pale; they often complain of headache; pain referred to the loins is less common than might be supposed. There is usually complaint of weakness; the tongue is generally clean, and the bowels almost invariably confined. The last circumstance is important in connection with the influence which constipation was proved by Mahomed to have on the development of scarlatinal nephritis. It is probable that there are many cases of acute nephritis which remain latent and get well, and many more would do so but for such an accident as a chill to the surface, or constipation.

Dropsy.—More or less œdema is commonly present in acute nephritis, but it is less constant than has been stated. It is notably absent in the majority of cases occurring in the course of acute diseases. The most frequent exception to this rule is scarlatina, in which the presence of dropsy often draws attention to a nephritis which in many other acute diseases would pass unrecognised.

The amount of dropsy varies very much, from mere puffiness

of the eyelids to general anasarca with effusion into the serous sacs.

The eyelids are the most constant seat next the lower extremities, then the trunk, scrotum, etc.

Œdema of the conjunctiva is a common symptom of Bright's disease, giving the eye a peculiar lustre.

Œdema of the lungs and glottis are complications which will be described hereafter.

Temperature.—The onset of acute nephritis does not seem to be attended by any marked inflammatory fever. The temperature in cases seen early in their course is sometimes 100°, but after a few days it becomes normal or subnormal, and does not rise except on account of some complication.

Heart.—The heart is liable to attacks of acute softening or myocarditis, in which it may become rapidly dilated, and this dilatation may be followed by rapid hypertrophy. As a rule the left ventricle is alone affected. The enlargement of the heart leads to displacement of the apex beat outwards, and a systolic murmur may be audible over it. In other cases the first sound at the apex is reduplicated, and the second sound in the aortic area accentuated. These alterations are the result of the increased pressure in the aortic system, causing delay in the systole of the left ventricle followed by rapid and abrupt closure of the aortic semi-lunar valves.

Blood.—According to Lloyd-Jones the density of the blood is very much reduced, being only 1032 instead of the normal 1058-60.

Pulse.—The rate of the pulse is at first quick, ninety to a hundred, but falls after the first few days to seventy or eighty, not seldom to sixty. The pulse is usually moderate in volume and not perceptibly hard, but the sphygmograph shows a characteristic curve of high tension (*Fig.* 15). In explanation of this discrepancy I would repeat my former remark that this curve is not really a measure of blood pressure, but of the duration of the tidal wave, which depends upon two factors, the peripheral obstruction and the force of the ventricle; whenever the former is too much for the latter the curve of high tension is produced, though in reality the ventricle may be weak and the intra-vascular pressure below normal.

Fig. 15. High tension pulse tracing of acute nephritis. The curve above the line *a b* is the full tidal wave.

Ophthalmoscopic appearances.—The fundus of the eye presents no change in acute Bright's disease of infective origin; except perhaps œdematous swelling in uræmic amaurosis.

Urine.—The *quantity* of urine is always reduced, at any rate for the first few days; it is generally under 30 oz., often under a pint in twenty-four hours.

The *density* is generally over 1020, often higher; in fact some of the densest urines are met with in acute scarlatinal nephritis, a sp. gr. of 1065 having been recorded in one instance (W. G. SMITH).

The *reaction* is almost invariably acid, unless affected by drugs. The *colour* and *translucency* depend mainly upon the amount of blood present; thus the urine may vary from being merely smoky through various shades of reddish brown to the colour of porter. If blood is present in very small quantity the urine may be yellow and clear.

The *deposit* is always considerable, consisting of mucus, epithelium, casts and blood; its colour and consistence vary from white and flocculent up to chocolate and dense, the principal factor in the change being the amount of blood present.

Uric acid crystals, urates of soda, potash and ammonia, or triple phosphates sometimes occur in the deposit.

The *urea* is generally under two per cent., often little more than one per cent.; so that as the quantity of urine is small the total eliminated is usually under two hundred grains *per diem*.

Albumen is often not very abundant. A dense cloud is a fair description of the amount; more accurately from ·05 to ·1 per cent., but in severe cases it may reach one per cent. or more.

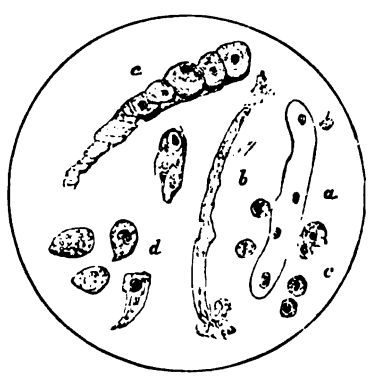

Fig. 16. *a*, Deposit in acute nephritis showing slender hyaline cast; *b*, mucous cylinder; *c*, hyaline and epithelial cast; *d*, pear-shaped epithelial cells from pelvis of kidney; *e*, epithelium from tubules.

Willey has shown that acute nephritis is often found *post mortem* in scarlatinal cases which have presented no albuminuria during life.

Blood is most constantly present, generally in large, sometimes only in small amount; it often persists for long and

recurs in a troublesome manner. The *casts* most commonly seen are blood and hyaline, the most significant are epithelial.

Epithelial cells are usually abundant. The following may be taken as a typical report of the urine of an ordinary case of acute nephritis :—

Urine 10 oz. ; sp. gr., 1020 ; acid ; smoky ; brownish deposit ; urea, 1·2 per cent. ; albumen, ·2 per cent. ; under microscope deposit contains epithelial, hyaline, granular and blood casts, red and white blood corpuscles and abundant renal epithelium.

DIAGNOSIS.—Even when dropsy is absent, if the urine is scanty, albuminous, and contains blood and epithelial casts, acute nephritis may be safely diagnosed. The difficulty is to distinguish between acute nephritis in previously healthy kidneys and an intercurrent attack in the course of chronic nephritis. This can be only determined with certainty by the history, but the age of the patient is suggestive. Thus in children primary disease is very common, while after forty years of age it is very rare. The presence of albuminuric retinitis or hæmorrhages indicates latent contracting kidneys, as does also, though with less certainty, the discovery of distinct enlargement of the heart early in the case. In intercurrent acute attacks the quantity of urine rapidly rises to normal or more than the normal amount.

COMPLICATIONS.—Primary acute attacks are not attended by many complications, but a mild degree of *uræmia* is often present giving rise to *headache* and *vomiting*. *Convulsions* sometimes occur even in mild cases in children, and these may be followed by *coma*. *Œdema of the glottis* is a localisation of the dropsy attended by special risk on account of its seat at the opening of the air passages.

DURATION.—It is not easy to fix the exact duration of an acute attack. The more urgent symptoms usually cease in two or three weeks under suitable treatment, but the kidneys are so far damaged that albuminuria continues as a rule for many months, during which the patient is in imminent danger of a relapse. If the symptoms persist beyond six weeks, the case is usually regarded as becoming sub-acute or chronic. Our language in this respect is defective, and it is plain that no very hard and fast line can be drawn.

PROGNOSIS.—The chances of recovery from an acute primary attack are decidedly favourable. Death rarely occurs during the acute stage. It is not easy to speak so confidently as to the ultimate result. A large proportion no doubt gets quite

well; in a certain number the kidneys remain damaged sufficiently to render them very liable to fresh attacks; while others become chronic. In all cases the utmost care is needed, and an opinion as to the ultimate result must be very guarded until months have elapsed and all trace of albumen has disappeared from the urine.

If this account of the prognosis of acute nephritis should appear to some to be too favourable, I would remind them that we recognise the disease much more commonly and in milder phases than was formerly the case. Thus Thomson's statistics show, that out of a hundred and eighty cases of scarlatina, one hundred and twelve, or 63·2 per cent., were affected with nephritis; that is to say the urine contained albumen, blood and tube casts, but only twenty-four showed any anasarca. Of the hundred and twelve only eleven died, of whom four are stated to have died from malignant scarlatina. One died from uræmia. Of the eleven fatal cases only five showed any anasarca, though two cases in which this was noted as abundant were fatal. The case that died from uræmia had only slight dropsy.

These figures show that the majority of cases, even of post-scarlatinal nephritis, when properly cared for, do well.

The guides to an opinion as to the probable termination of the case should be (1,) The evidence of the functional power of the kidneys as shown by the daily amount and character of the urine; (2,) The degree of dropsy present.

ILLUSTRATIVE CASES.

CASE 4.*—*Acute Bright's disease following sore throat (tonsillitis?); persistent hæmaturia.*

George T., aged twelve, schoolboy, admitted March 4th, 1887, with weakness and hæmaturia.

Eight weeks ago he had a sore throat, and after he had got over that he began to swell. His grandmother, with whom he lived, thought he had got a chill going to school. His family history was imperfect, but negative so far as it could be ascertained; his parents were not supposed to be dead. His previous health was good, but he had had scarlatina and measles when a baby. He was a fairly healthy looking boy, with rather a puffy face; skin dry and brown; slight œdema of the legs. T. 100°; P. 78; R. 18; tongue dry, white; appetite good; no pain after food, or vomiting; bowels confined (he said they were regular); liver and spleen normal; no ascites. Heart's apex in fifth interspace inside nipple line;

* Recorded by Mr. Ross Jordan, Clinical Assistant.

a systolic murmur at apex, with accentuation of the second sounds at the base. Pulse irregular; lungs normal.

No lumbar pain; says he gets up in the night to make water; urine 14 oz.; sp. gr. 1014; acid; contains albumen and blood.

March 12th. Œdema has disappeared.

March 13th. Urine 16 oz.; sp. gr. 1017, acid; dark smoky red colour; dark reddish brown deposit; urea ·95 per cent.; albumen quarter column; epithelial granular and blood casts, red and white blood corpuscles, squamous epithelium, uric acid, and granular matter in deposit.

This condition of urine continued for two months, except that the quantity was, on an average, normal. He was not discharged till June 13th. The last urine report is as follows: Urine 35 oz.; sp. gr. 1016; acid; straw colour, slightly turbid; reddish white flocculent deposit; urea 2 per cent.; a cloud of albumen; a trace of blood; granular and epithelial casts, red and white blood corpuscles, squamous epithelium and uric acid. He was made an out-patient, but did not attend.

CASE 5.*—*Acute Bright's disease; uræmia; recovery.*

John B., aged six, schoolboy, admitted April 3rd, 1886, with swelling of legs and face. He had been ill a week. Four years and a half previously he had scarlatina, not followed by dropsy; two of his brothers had it at the same time.

He was a well nourished child with a pale swollen face, and considerable anasarca of the trunk and lower extremities; his eyelids were puffy. T. 98°; P. 102; R. 24. Tongue slightly furred; bowels confined; no ascites. Liver and spleen normal. Heart's apex in fifth intercostal space just external to the vertical nipple line; a faint systolic murmur was audible in the mitral area, but the heart sounds elsewhere were loud and accentuated. Pulse small, regular, rather hard. Breath sounds rather feeble posteriorly; lungs otherwise normal.

Ophthalmoscopic appearances normal. Urine, 16 oz. in 24 hours; acid; sp. gr. 1018; in colour and appearance like beef tea; 1½ in. of brown deposit; urea, 1·3 per cent.; albumen, 0·17 per cent.; blood in large amount. Epithelial, blood, hyaline, and granular casts, with blood corpuscles and renal epithelium in deposit.

He was put on milk diet, and treated by diaphoretics and diuretics.

April 12th. The œdema of the legs has disappeared.

April 17th. Hæmaturia still abundant; ordered ext. ergotæ liq. ℥v, *quartis horis.*

April 23rd. Blood reaction with guaiacum and ozonic ether feeble.

April 27th. He had an attack of uræmic convulsions which lasted an hour and a half, but not attended by loss of consciousness.

After this attack his pulse fell to 60, and was labouring, irregular and intermittent.

April 28th. Ordered solution of nitro-glycerine (1 per cent.), ℥j, *secundis horis.*

May 13th. He was much better; the pulse still intermits at long intervals; he was allowed to get up.

June 4th. He had been going on very well, when the hæmaturia recurred.

June 12th. By this time the blood was nearly gone.

* Recorded by Dr. Stacey Wilson, House Physician.

July 8th. He was discharged free from œdema, and in fair health; urine 30 oz.; amber; acid; slight flocculent deposit; urea 1·7 per cent.; albumen ·05 per cent.; an occasional hyaline cast and a few blood corpuscles in the deposit.

Urine of John B., acute nephritis :—

Date.	Quantity of urine in oz.	Quantity of urea in grains.	Quantity of albumen in grains.	
April 5th ...	16	91·52	119·6	
„ 12th ...	16	147·84	70·4	
„ 19th ...	14	117·04	30·8	
„ 23rd ...	16	112·64	14·0	
„ 28th ...	20	123·2	44·0	
May 3rd ...	16	105·6	7·0	
„ 12th ...	24	137·28	10·5	
„ 19th ...	36	237·6	15·8	
„ 25th ...	30	145·2	13·2	
June 2nd ...	30	198·0	6·6	
„ 7th ...	30			Too little to estimate.
„ 9th ...	30	118·8		
„ 16th ...	22	92·4		
„ 23rd ...	40	191·2		
„ 27th ...	26	193·48		
July 8th ...	30		7·0	Urea not estimated.

CASE 6.*—*Ulcerative endocarditis; sub-acute infective nephritis; uræmia. Death. Autopsy.*

E. S.——, female, eighteen, domestic servant, admitted July 2nd, 1886, complaining of pain at the heart and swelling of the legs and face. For the last four months she had been ailing, but her legs began to swell fourteen days before admission. She had had rheumatic fever three times in the last five years. Her previous health was good.

Father died of phthisis, aged forty-eight. Mother died of heart disease, aged forty-nine. One brother died of heart disease, aged thirteen. Two died in infancy; four are living and in good health. Patient has marked œdema of eyelids and face, slight œdema of legs and ankles; T. 100°; P. 96; R. 30; tongue clean; digestion good; bowels regular; liver and spleen not enlarged.

Heart's apex beat in fourth left interspace, internal to nipple line, but dulness extends half an inch beyond the nipple in the fifth interspace. A loud systolic murmur in the mitral area; pulmonary second sound loudly accentuated. Pulse small, but not easily compressed.

Lungs normal, except some dulness with deficient breath and voice sounds at left base.

She has not menstruated for six weeks.

Has no pain or difficulty in making water.

* Recorded by Dr. Stacey Wilson, House Physician.

Urine, 26 oz.; 1014, acid; straw-colour, blood-tinged; reddish deposit; urea, 1·4 per cent.; a cloud of albumen; numerous hyaline and granular, with a few colloid and epithelial casts, red and white blood corpuscles, squamous and renal epithelium, and uric acid crystals.

After admission her temperature assumed a hectic type, rising at night sometimes as high as 103° Fahr. Her urine remained much the same.

On August 10th she became drowsy, and this was followed by uræmic convulsions. Two days later the convulsions returned, coma supervened, and she died.

Autopsy performed by Dr. Crooke.

Subject emaciated; features pale and puffy; lips livid; feet and ankles swollen. Abdomen distended.

Heart, 11½ oz., pericardium universally adherent by old fibrous adhesions; both ventricles dilated, the left especially. Left ventricle contains dark semi-fluid blood clots; watery fluid blood, and colourless soft clot in right auricle and ventricle; valves in right side normal.

Aorta, rather narrow, valves normal. Extensive recent endocarditis round mitral valve extending into left auricle on its outer wall, where there is a large patch of vegetations. The mitral curtains are beset with soft greyish friable vegetations. Wall of left ventricle vascular, cloudy, mottled yellow in places, soft and friable.

Lungs congested in their lower lobes; upper lobes œdematous.

Liver 56 oz., soft, pale, with hyperæmic patches.

Spleen 13½ oz., adherent, contains a large infarct which is breaking down, and another smaller one softening in the centre.

Several hæmorrhages in spleen substance, which is very vascular.

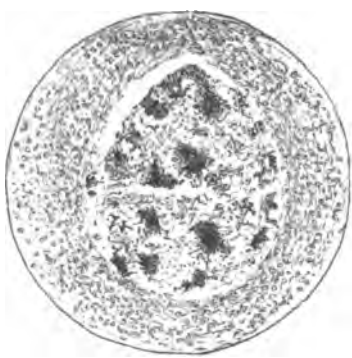

Fig. 17. Malpighian Body from case of subacute nephritis in ulcerative endocarditis, showing infiltration of the tuft with micro-organisms (streptococci).

Kidneys 9 oz., capsules strip easily, leaving a characteristic greyish brown and red speckled surface. On section the cortex is increased, presenting the same finely mottled, grey brown and red coloration, mixed with a sprinkling of yellow.

The cut surface is dotted with whitish points, which are the glomeruli altered by inflammatory change. At the inferior end of the left kidney is a small wedge-shaped infarct, yellowish white, dry looking and firm, fringed with a zone of hyperæmia. The medullary cones are uniformly light chocolate brown in colour. Under the microscope the Malpighian bodies are infiltrated with micro-organisms, chiefly *streptococci* (*Fig.* 17).

TREATMENT.—The main lines of treatment are rest and warmth, aided by suitable diet, purgatives and diaphoresis.

The patient should remain in bed, in a flannel night-dress, wrapped in a blanket, or the sheets may be taken off the bed. The diet should be *milk* and farinaceous food. No beef tea (according to Masterman, beef tea is analogous in chemical

composition to urine except that it contains less urea and uric acid), meat extracts or jellies should be given. The bowels should be kept open by an occasional purgative (bitartrate of potash ʒss, honey or treacle ʒj), every second or third day if required. The best diaphoretic is the ***hot air bath***, which should not be prolonged beyond twenty minutes. It will be found that a patient who does not sweat at all in the bath on the first few occasions will do so perfectly well afterwards. The hot air bath may easily be improvised by a spirit lamp set under a stool or cradle in the bed, if one of the cheap tin lamps sold for the purpose is not available. I very much prefer this method to the hot pack, which has been shown by Goodhart to be dangerous by causing pyrexia. I have had the temperature taken many times before and after the hot air bath, and have not noticed any rise.

I usually give a pint of Imperial (potassii bitart. ʒss., sacch. alb. q.s., aquæ Oj,) daily as a drink, to keep up the alkalinity of the blood serum and diminish the acidity of the urine, nor have I seen any reason to believe it harmful, in spite of the theoretical importance of potassium salts in the pathogenesis of uræmia.

Great responsibility attaches to the medical attendant with respect to the care and conduct of his patient after convalescence is reached. Undoubtedly great, sometimes insuperable difficulties are placed in his way, but it is his plain duty to point out as impressively as he can the dangers that lie ahead and the precautions needed to avoid them.

The patient must be told of the great liability there is for the disease to relapse from exposure to cold, from injudicious diet, and from the occurrence of any infective disease, however slight.

If possible he should spend the winter in a milder climate than our own, or in the mildest parts of this island. He should not be allowed to eat butcher's meat or cheese, or to drink alcohol in any form until all albumen has disappeared from his urine, and even then he should be warned to use these articles of diet very sparingly.

His dress should consist of underclothing of wool from head to foot, summer and winter, and he should be prevented from taking part in work or exercise likely to overheat his body or risk the possibility of a chill.

CHRONIC INFECTIVE NEPHRITIS.

ETIOLOGY.—As a result of neglect of proper precautions after an acute attack, often in ignorance of its existence, the patient gets a chill, and a fresh attack is lighted up which may pass into chronic nephritis. Moreover such kidneys are specially liable to be irritated by the various poisons which can set up nephritis in healthy kidneys.

In chronic infective diseases there is a correspondingly chronic nephritis which often remains latent for a considerable part of its course.

MORBID ANATOMY.—As a rule the kidneys become larger and paler; the capsule still strips off readily, leaving a smooth shining surface. On section, the cortex is broad, white, and soft, while the pyramids are pale red and streaked with white lines. The Malpighian bodies often show the reaction of lardaceous or waxy degeneration with liq. iodi. In its most pronounced type this constitutes one form of the "large white kidney," but this anatomical variety may originate in other ways.

In some cases the kidney is no larger than normal or may be even smaller, and instances have occurred in which one kidney is large and the other small, as in the following description of a pair of kidneys copied from the *post mortem* register of the General Hospital.

Kidneys of H.—The right is enormously swollen, and weighs 14½ oz., while the left is much smaller, weighing only 6 oz., and is much lobulated. Both are pale, soft and flabby in consistence, capsules easily separable, leaving a dull white ground colour mottled with red and yellow (branny kidney). On section, the *right* or larger kidney presents large white areas in which the fatty changes (yellow branny speckling) are marked: the cortex is much increased in breadth, of a uniform grey white colour, swollen, generally opaque, but in some places semi-translucent in appearance, showing also a fine yellow speckling of the surface, and streaked and dotted with lines and points of hyperæmia. The *left* or smaller kidney presents very similar appearances except that it is rather more vascular; no difference can be felt in its resistance to the knife, and it is as soft and doughy as the right kidney. At the bottom of the depressions or lobulations the capsule appears slightly thickened and adherent, and a small greyish semi-translucent strand appears to enter the cortex.

In other cases, especially in post-scarlatinal kidneys, in which interstitial nephritis was noted as occurring during the primary acute attack, the organs are reduced in size, with thickened and adherent capsules, and pale roughened surfaces. On section, the kidney substance is abnormally tough, while the cortex is narrowed. The atrophic stage may come on

rapidly, marked examples having been met with at the end of two months (EISENLOHR).

This is the type which was formerly described as a third stage, in which the large white kidney had undergone atrophy, but it is now thought more probable that these kidneys have never been much enlarged, and that interstitial inflammation has been a marked feature in the inflammatory process from the beginning. It is not clear under what circumstances, apart from the clinical fact of its frequency in scarlatina, this particular form is developed. As already mentioned, Grawitz and Israel found the two types of kidney occurring in animals indifferently as the result of artificial nephritis induced by temporarily occluding the renal artery.

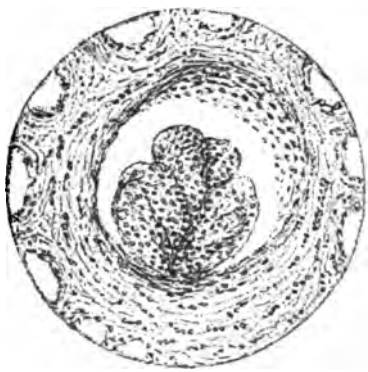

Fig. 18. Malpighian body showing marked peri- and endo-capsulitis, with increase of the nuclei of the tuft.

Histology.—The *Malpighian bodies* present hyaline change of their capillaries. The capsules frequently show marked peri-capsulitis, being swollen and broadened out by concentric bands of nucleated fibres; while their endothelium is proliferated, sometimes forming a mass of granulation tissue (*Fig.* 18), encroaching on the tuft. The *blood vessels* are dilated and full of clot; they are often thickened by hypertrophy involving all the coats. The *convoluted tubes* are dilated, their epithelium is fatty, only the basal portion being left (*Fig.* 19). The cavities of the tubes contain fat granules and epithelial débris. The *straight tubes* of the medulla.

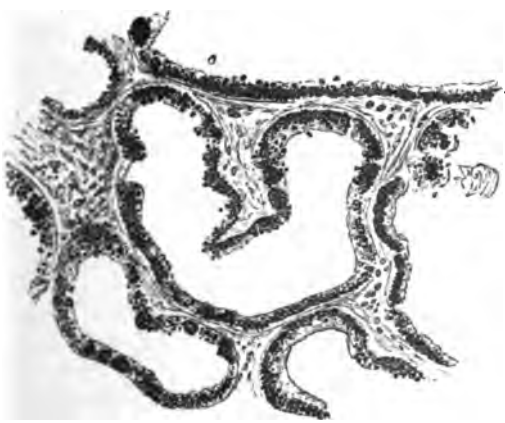

Fig. 19. Osmic acid preparation showing marked atrophy and fatty degeneration of the epithelium of the convoluted tubules.

preserve their epithelium, but their cavities often contain casts made up of fatty granules and epithelial débris from the convoluted tubes. The *stroma* is everywhere swollen, nucleated and hyaline.

These changes indicate a diffuse inflammation of the glomeruli, coats of the blood vessels, and stroma, with fatty degeneration of the previously inflamed epithelium of the convoluted tubes.

The microscopical examination of the pair of kidneys, whose naked eye appearances were described above, showed that the difference between them consisted in the presence in the smaller kidney of large areas of nucleated fibrous tissue, enclosing atrophied tubules.

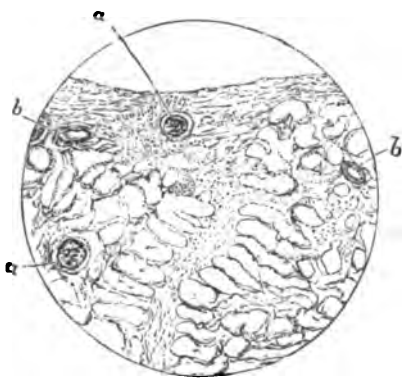

Fig. 20. Section of kidney from chronic infective nephritis brushed out so as to show the thickened stroma.

Fig. 20 is a preparation from such a kidney brushed out so as to remove all but the framework of connective tissue. In the centre of the section there is a wedge-shaped process of nucleated connective tissue enclosing a Malpighian body (*a*). This corresponds to the vascular zone, and it is in the neighbourhood of the interlobular arteries and around the Malpighian bodies, that the growth of connective tissue is most marked. But the intertubular stroma is everywhere swollen and thickened. The thickening of the walls of the blood vessels in such kidneys is always correspondingly well marked.

SYMPTOMS AND COURSE.—*Dropsy.*—There is no form of Bright's disease in which dropsy is a more constant accompaniment. It is rarely but occasionally absent. As a rule it is most usually present in the face, feet, and legs, but there may be general anasarca with effusion into the serous sacs.

Heart.—The heart is generally hypertrophied, that is to say, the apex beat is displaced outwards. A systolic murmur is often heard at the apex; when this is absent there is reduplication of the first sound, and the aortic second sound is accentuated.

Blood.—The density of the blood is not so much reduced as in the acute form, owing no doubt to the larger elimination of water from the kidneys. Lloyd-Jones gives it as 1049 against 1058-60, the density of normal blood.

Pulse.—The pulse is usually about sixty, and incompressible. The sphygmographic tracing (*Fig.* 21) shows the character of high tension very well, though this particular instance illustrates the statement already made, that the curve of high tension represents only the prolonged systole resulting from the effort of the ventricle to overcome the peripheral obstruction, as it was taken from a case where the heart was failing rapidly.

Fig. 21. High tension pulse tracing from case of chronic febrile nephritis.

Ophthalmoscopic appearances.—According to my experience these are normal in undoubted cases of chronic nephritis belonging to this class. If changes occur they do so very rarely.

Urine.—The *quantity* of urine is generally increased, being from sixty to ninety ounces *per diem.* It is usually *acid;* of a *density* of 1010 to 1015; the *urea* varies from ·7 to 1·5 per cent., the daily quantity being from two hundred to three hundred grains; the albumen is generally considerable in amount, from ·4 to 1 per cent. or more; blood in traces is commonly present; numerous epithelial, fatty, granular, and hyaline casts are visible in the deposit, together with red and white blood corpuscles and fatty renal epithelium.

Headache and *vomiting* are of frequent occurrence. *Convulsions* and *coma* and other symptoms of *uræmia* are less common than in the acute attack, and much less than in the contracting kidney with which they are specially associated, and where they are described fully.

DIAGNOSIS.—When dropsy is present, and the urine is copious, highly albuminous, and deposits numerous casts and renal epithelium, this form of Bright's disease is suggested. The diagnosis may be made quite plain by the history. If this is wanting it may be difficult to decide, as after one or more intercurrent acute attacks the clinical symptoms of lithæmic kidney are so modified as to make the differentiation almost impossible. The presence of retinal changes indicates lithæmic kidney. The age of the patient is of importance, as the latter disease is very common after forty years of age,

while primary acute nephritis and its sequelæ are relatively rare.

DURATION.—The disease always lasts months, and may last years. A gentleman well known to me had an attack of scarlatinal nephritis thirty years ago. According to his medical attendant his urine always has presented the characters which I have observed in it during the last few years. It contains a large amount of albumen with epithelial, fatty, granular, and hyaline casts. It is possible that the disease in this case affects only one kidney or a portion of one, for such cases have been known to occur. At any rate, it shows that persons presenting the urinary signs of chronic nephritis after an acute attack may go on for half a lifetime. This gentleman is now aged forty-six; he enjoys fair health, and, although he leads a careful life, he takes ordinary diet, with a moderate amount of wine.

PROGNOSIS.—Although these cases may last a long time, the prognosis must be very guarded, as they are certainly very precarious lives. As a rule they recover sufficiently to go about, but they are very liable to relapse.

The worst prognostic sign is extensive and obstinate dropsy.

ILLUSTRATIVE CASES.

CASE 7.* *Phthisis; chronic infective nephritis; lardaceous degeneration. Death. Autopsy.*

T. T.———, æt. thirty-seven, gun finisher, admitted April 6th, 1886, complaining of cough, pain in chest, scantiness of urine, and inability to take solid food. He spits a good deal and the sputa have been once or twice streaked with blood.

He has had a cough for eighteen months, and has gradually got weaker, and lost flesh. Six weeks ago diarrhœa set in, and reduced him greatly. He attributes his illness to repeated colds. His work exposes him to dust, but not to cold or damp.

His father, aged sixty-three, is at home suffering from his lungs, but his mother and all his brothers and sisters are alive and healthy.

Present condition.—Patient is a sallow, poorly nourished man; legs and feet œdematous. T. 100°; P. 96; R. 18; tongue clean, red and dry; suffers from flatulence, pain between shoulders, and nausea. Bowels confined. Vertical liver dulness six inches in mammillary line. Spleen not enlarged.

Heart's apex in fifth intercostal space, where there is a faint systolic murmur; first sound reduplicated in tricuspid area; second sound in pulmonary area accentuated and reduplicated.

Pulse small, regular, soft and compressible; voice weak; phonation not painful; cough troublesome; sputa copious, mucous and frothy.

* Recorded by Dr. Stacey Wilson, House Physician.

Dulness at both apices, more marked on the right side. Bronchial breathing heard above right clavicle, and whispering pectoriloquy all over right upper lobe. Everywhere else respiration indeterminate, with scanty crepitations.

Urine seventy-six oz.; sp. gr. 1008; acid; bright amber colour; mucous deposit; urea ·6 per cent.; a faint cloud of albumen; hyaline casts and leucocytes in deposit.

A sphygmographic tracing showed that the tidal wave was prolonged in spite of the weakness of the heart.

The œdema of the legs at first disappeared, but it returned by April 21st. He got gradually worse. The quantity of urine remained large and the albumen increased in amount.

He died on May 14th of a sudden attack of dyspnœa.

AUTOPSY, May 14th.—*External Appearances.*—General pallor and emaciation; œdema of feet and legs.

Lungs, adherent; honeycombed with cavities, but especially the upper lobe of the right lung; bronchi dilated, containing pus and surrounded by indurated areas. Small patches of grey miliary tubercle scattered through lungs. Both bases congested and œdematous.

Heart, 13 oz.; *left* ventricle dilated and hypertrophied; soft reddish vegetations on aortic valve and on aortic segment of mitral valve.

Peritonæal cavity full of fluid.

Liver, 67 oz.; smooth, tense, edge rounded, colour dull brown; on section, translucent, gave waxy reaction with iodine.

Spleen, 8 oz., a typical "sago spleen."

Kidneys, 9 oz.; capsules partly adherent; surface pale yellowish white, with well defined stellate veins on surface. On section, cortex of normal width; mixed greyish white and yellow in colour; rather anæmic, translucent and shining, giving the iodine reaction distinctly. The mucous membrane of the whole alimentary canal gave the reaction with iodine, but the muscular substance of the heart and tongue was normal.

CASE 8.*—*Chronic infective nephritis; great improvement.*

Henry M., aged nineteen, warehouseman, admitted March 22nd, 1886, with swelling of the face, feet, and legs. He had been ill since November, 1885, when the swelling began, and he was told at the Dispensary that he had Bright's disease.

He had scarlatina when he was four years old, but no other definite illness.

His father, mother, and six brothers and sisters were all healthy.

On admission he looked very anæmic, with a pale puffy face, and considerable œdema of the feet and legs. T. 98°; P. 72; R. 18; tongue furred; bowels confined; liver and spleen are a little enlarged, the latter can be felt below the ribs.

Lungs, resonance deficient, at both apices; cog-wheel respiration; no accompaniments or cough. Heart's apex three-quarters of an inch external to verticle nipple line in fifth intercostal space. Sounds in mitral area very loud. A systolic murmur audible in aortic area, faintly conducted into vessels of neck. Aortic second sound accentuated.

Pulse full, of high tension, artery feels thickened.

* Recorded by Dr. Stacey Wilson, House Physician.

Ophthalmoscopic appearances normal.

Urine 60 oz.; sp. gr. 1015; acid; pale yellow colour, smoky; mucous deposit; urea 264 grains *pro die*; albumen '4 per cent.; blood in quantity; fatty epithelial, hyaline and granular casts, with blood corpuscles and fatty epithelium in the deposit.

He made fair progress; he was kept in bed till May 14th, when the œdema had entirely disappeared. On being allowed up it returned slightly in the legs. He was discharged on July 2nd to go to the Sanatorium, and from there he went to take a situation in the South of England, whence he wrote to say that he was going on very well.

The following table marks his progress :—

Date.	Urine in oz.	Sp. gr.	Albumen in grs.	Urea in grs.	Casts.
Mar. 24	60	1015	105	264	Epithelial, hyaline, fatty & granular
„ 30	56	1015	81	369	„ „ „ „
April 8	72	1015	126	285	„ „ „ „
„ 15	70	1016	308	277	„ „ „ „
„ 22	72	1015	169	221	„ „ „ „
„ 27	70	1015	184	215	Hyaline, fatty, and granular
May 7	76	1013	200	299	Epithelial and hyaline
„ 13	72	1012	253	223	Few hyaline and granular
„ 19	80	1014	150	352	Epithelial, fatty and hyaline
„ 25	76	1016	133	334	„ „ „
June 2	84	1014	221	332	Epithelial and hyaline
„ 9	74	1015	162	205	„ „ „
„ 16	84	1015	147	221	Epithelial, hyaline, and fatty
„ 23	76	1015	133	367	Hyaline and few granular
„ 30	76	1014	133	334	Hyaline

TREATMENT.—The patient must be kept in bed, clothed in flannel, in a room the temperature of which is carefully regulated by day and night to avoid chills, and he should be kept in bed so long as any dropsy remains, though slight swelling of the legs coming on after he is allowed up does not necessarily call for a return to bed. The diet should be at first milk, with bread and farinaceous puddings, white fish and poultry being added as the case progresses satisfactorily. Butcher's meat and cheese should be forbidden so long as the doctor has control of the case. No alcohol should be permitted.

The treatment should be chiefly directed to getting rid of the dropsy by diuretics, purgatives, and diaphoresis.

The *hot-air bath* should be used daily. An electuary of bitartrate of potash and honey should be taken freely so as to

act upon the bowels, combined with a diuretic pill such as the following:

℞ Pulv. digitalis
Pulv. scillæ
Caffeinæ citratis, āā gr. j.
Ft. pil.
Sig. One to be taken thrice daily.

If the dropsy is very great, speedy relief may be obtained by tapping. If there is much ascites this should be done at once. Tapping the legs by the small trocars introduced by Southey is not a very satisfactory proceeding. The fluid drains away so slowly that the dropsy may not be affected by it. This practice is sometimes successful, but it is not one of which I can speak very highly, and I get much better results from massage and bandaging.

When convalescence appears to be established iron should be given, preferably the carbonate, citrate or tartrate.

The precautions to be taken by the convalescent are the same as those already detailed for the acute attack; he should especially guard against acquiring the uric acid dyscrasia.

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CHAPTER XI.

LITHÆMIC NEPHRITIS.

(SYN. GOUTY KIDNEY.)

THE most common form includes a number of cases of acute nephritis, *e.g.*, those occurring in gout, and such instances as that of a habitual beer drinker, whose blood is loaded with uric acid, meeting with a severe chill, his kidneys being already more or less irritated or actually altered by the dyscrasia; as well as the very common intercurrent acute attacks which occur during the course of the chronic process. But the very great majority are chronic cases of the clinical type associated with the small red granular kidney, although it is a mistake to suppose the disease is limited to one anatomical type

ETIOLOGY.—As the name implies, it is primarily due to the presence of a poison, *e.g.*, uric acid, in the blood and to the prolonged effect of its elimination through the kidneys.

Age.—It is rare under twenty years of age, less rare up to forty, becomes common after that period is passed, and after fifty is so common that nearly one-third of all persons dying above that age show more or less signs of its action in their kidneys.

Sex.—All statistics agree in showing that the contracting type of kidney is less common in females than in males. This is true, but the truth would be more striking if the figures were not vitiated by two circumstances, namely, the frequency of contracting kidney of obstructive origin in women with pelvic diseases, and, secondly, the fact that contracting kidney may be of infective origin.

Nevertheless, I accept the figures for what they are worth. Dickinson gives the proportion of one female to two males; Wagner, of fifty-five females to ninety-five males. We are not told whether the numbers were calculated out so as to show the proportion to the total deaths in each sex. This is important, as out of a hundred cases collected without refer-

ence to etiology from the General Hospital registers, I found thirty females to seventy males, but there were only a hundred and thirty-six female deaths to three hundred and four male deaths, so that the percentages brought the figures very near, namely, twenty-two females to twenty-three males.

But on the other hand, the relative infrequency of this form of Bright's disease in females is an incontestable clinical fact.

Temperament.—The doctrine has been favoured by authority that nervous worry is a cause of contracting kidney, but in my opinion it is the uric açid diathesis which is so often associated with an irritable nervous temperament, the subjects of which are prone to worry.

Social condition.—It attacks all classes, but is especially common among workers in lead, miners, brewers, publicans, forgemen, and stokers.

Heredity.—There should be no doubt of the existence of a hereditary tendency to this disease. In the case already quoted, as seen with Dr. Lycett, it was this form of Bright's disease from which the patient, his father, and two paternal uncles died.

Eichhorst has related the history of a family, in which the grandmother, mother, two sons and a sister suffered from this disease.

Mahomed believed in the existence of a diathesis—Bright's diathesis—closely allied to gout, and presenting the following characteristics: "Habitual constipation, some forms of dyspepsia, often signs of imperfect circulation, such as cold hands and feet, not unfrequently palpitation, sometimes shortness of breath on exertion. Their skins are often thick, of velvet-like softness, and very white." This quotation is given merely to indicate Mahomed's line of thought. So far as my clinical experience goes, I cannot say that it confirms his description of the characteristics of the individuals in whom we commonly meet with this form of Bright's disease, nor am I able to suggest a better one, though I incline to the opinion that the spare neurotic type is especially prone to suffer from lithæmic kidney.

Dieulafoy also believes in a "diathèse brightique," of which the signs are: 1, auditory troubles, noises in the ears, Menière's vertigo; 2, asphyxia of the extremities, fingers pale, bloodless, and numb; 3, itching; 4, pollakiuria or frequent micturition; 5, cryæsthesia or sensitiveness to cold; 6,

cramps in the calves of the legs; 7, epistaxis; 8, electriform shocks at the moment of falling asleep; 9, distension and tortuosity of the temporal artery. But he does not suggest that they are all constantly present, or that any one by itself is pathognomonic.

Climate.—The mode in which our moist cold climate predisposes to Bright's disease has been already explained.

Garrod states that chilling the skin increases the formation of uric acid, while it probably gives rise to other alterations in the blood by diminishing elimination.

Gout.—There can be no doubt of the frequent association of these conditions. This was first pointed out by Todd, who gave to the renal disease the apt name of "gouty kidney."

Ebstein says that the kidneys may be perfectly healthy even when the articular affection is very pronounced; or they may be in a state of chronic atrophy with uratic deposits; or there may be uratic deposits in the canaliculi or in necrotic foci. He believes the deposit of urate of soda in necrotic foci alone is typical; he recognises the first stage as an inflammatory process set up by uric acid, and this is followed by necrosis, uratic salts being deposited in the cavities thus formed.

There is no necessary connection between articular gout and nephritis. The tendency to accumulate uric acid in the blood may exist apart from articular gout. It is known that the first metatarso-phalangeal joints of the subjects of this form of Bright's disease are generally the seats of uratic deposits, but a history of attacks of gout is exceptional. Both the joint affection and the kidney disease depend upon the accumulation of uric acid in the blood, but for the production of either there is needed the presence of special etiological factors.

Lead.—Ollivier originally drew attention to the frequent occurrence of the disease among lead workers. He proved that lead is eliminated by the kidney. We know, too, that lead leads to accumulation of uric acid in the system, either by depressing the function of the liver or by forming insoluble urates. There is a general agreement among clinical observers in this country as to its prevalence among patients in whom evidence is to be found of past or present poisoning by lead.

Charcot and Gombault succeeded in causing contracting nephritis in rabbits by the prolonged administration of lead.

Hard water.—Permanent hardness in drinking water, due to excess of lime salts, is an undoubted cause of the uric acid

dyscrasia in the persons who use it, and thereby it is an indirect cause of Bright's disease. Its *modus operandi* has not been clearly explained. Whether it acts by forming insoluble urates or by favouring by its presence the decomposition of soluble urates, are questions worthy of investigation. Throughout this district (Warwickshire, Staffordshire, and Worcestershire) the drinking water is very hard, and its relation to uric acid formations is to my mind beyond all question.

Alcohol.—Dickinson's criticisms of the alcoholic etiology of Bright's disease are entitled to great weight, but it is doubtful whether alcohol can be altogether acquitted. The observations of Glaser already quoted (p. 92), prove that its ingestion is immediately followed by signs of renal irritation.

Animal food.—The excessive use of *butcher's meat*, such as is common in this country, especially among certain classes of well-paid artizans, is generally and most properly believed to be a very powerful cause of this disorder. It acts by increasing the raw material from which uric acid is formed, and also (and this is perhaps as important) by the large amount of salts contained in it (chlorides, sulphates, and phosphates), which diminish the alkalinity of the blood, and prevent the solution of uric acid.

Dyspepsia.—Johnson has stated his belief in the frequent occurrence of this disease in persons who suffer from certain forms of dyspepsia, or who eat and drink to excess. Murchison was persuaded of its relation to the digestive derangement which he called "lithæmia," and associated with a functional deficiency of the liver. Mahomed published certain cases of young adults in whom dyspepsia was associated with albuminuria and high arterial tension, suggesting the belief that some products of faulty digestion were producing a dyscrasia, which affected the vascular system and irritated the kidneys in such a way as to lead in time to the development of contracting kidney with cardiac hypertrophy.

This is a view which I have fully accepted. It explains the occurrence of this form of Bright's disease in persons who are in no way given to excess, but whose digestive functions are inadequate, either congenitally or as the result of sedentary habits.

Heart Disease.—The relations of heart disease to the contracting granular kidney have been insisted upon by Dickinson, and a study of *post mortem* registers proves it to be a fact.

As has been often pointed out, the effect of heart disease is to approximate the mammal to the reptile, to diminish all oxidation processes, and to increase the formation of uric acid while diminishing that of urea.

MORBID ANATOMY.—Acute nephritis is not in itself a disease that often terminates fatally. We know it best in the infective form, where death is due to the primary disease. It is only in very severe cases that we get an opportunity of seeing the kidneys in acute lithæmic nephritis. They are then swollen, of a red or chocolate colour; the capsule strips readily off; on section blood drips from the cut surface, upon which the Malpighian bodies stand out as dark red points.

The condition is one of intense congestion, with acute catarrhal inflammation of the epithelium of the convoluted tubes.

In sub-acute cases the kidneys are still swollen, the cortex increased, pale and mottled; the capsules separate easily, leaving a pale marbled surface.

The changes are similar to those already described in sub-acute nephritis of infective origin. The epithelium of the convoluted tubes is swollen, granular, vacuolated and fatty; in places only a narrow band is left. The glomeruli are swollen, and their nuclei increased. The blood vessels are full of blood.

Still later, such kidneys may present the appearance of the large white kidney. They are greatly swollen, very pale, or mottled red, white, and yellow, soft, friable, capsules not adherent; on section the Malpighian bodies appear very distinct.

Under the microscope the epithelium is very fatty; the Malpighian bodies show well-marked glomerulitis; the blood vessels are dilated, and their walls thickened by hypertrophy and *endarteritis obliterans*; the connective tissue is swollen, hyaline and nucleated.

But the typical kidneys of this form of Bright's disease are the small red kidneys. They are small, weighing together less than eight ounces, hard, with opaque thick adherent capsules, which, when stripped off, tear the kidney substance, leaving a dark, red, granulated, often nodular surface, in which are a few small cysts varying in size from a pin's head to a pea. On section, the organ is tough; the cortical portion is dark red, dotted with vascular spots and divided from the medullary

cones by a well-marked line of hyperæmia; the cortex is very narrow, measuring often from $\frac{1}{8}$th to $\frac{3}{16}$ths of an inch in breadth. The medullary portion is purple, and the cones are striated with lines of hyperæmia. The mouths of the cut vessels are everywhere patent and stiff.

Under the microscope the following changes can be seen :—

Connective tissue.—If a thin section is brushed out so as to remove all but the frame-work of connective tissue, it will be seen that wedge-shaped processes of thickened and nucleated connective tissue pass down into the cortex from the capsule, occupying the region of the interlobular arteries and Malpighian bodies. The intertubular stroma is generally swollen and nucleated.

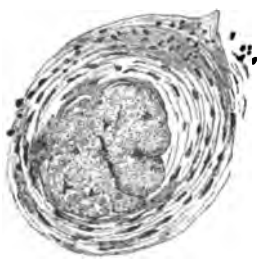

Fig. 22.—Malpighian body, showing well-marked capsulitis, with hyaline degeneration of the glomerular tuft.

Malpighian bodies.—The most general change is an increase in the nuclei of the capillary tuft and its conversion into a simple cellular mass. In a smaller number a later stage may be followed, in which the cellular mass becomes converted into delicate gelatinous tissue containing a few stellate cells (*Fig.* 22). Still later the contents undergo a complete colloid change so as to form a small cyst.

Blood vessels.—The capillaries are dilated and full of blood; in places they show concentric hypertrophy (*Fig.* 23). The larger vessels are dilated and their walls thickened. This thickening is most generally seen to affect the adventitia and the muscularis; the intima is thickened frequently, but not so constantly.

Fig. 23.—Capillary vessel showing concentric hypertrophy of its wall.

In the *adventitia* the change seems to be a purely inflammatory overgrowth which it shares with the neighbouring connective tissue with which it is directly continuous and forms part. The change in the *muscularis* is generally a true muscular hyperplasia, but in some vessels there is dilatation without hypertrophy, as might be expected. In the *intima* the elastic lamina is always swollen, its layers separated, and interspersed with a few nuclei; the endothelial layer is often normal, but sometimes there is a considerable overgrowth of tissue on the inner side of the elastic lamina evidently due to

inflammatory thickening of the endothelial layer. Such growths may cause irregular narrowings and even occlusion of vessels (*endarteritis obliterans*) (*Fig.* 24).

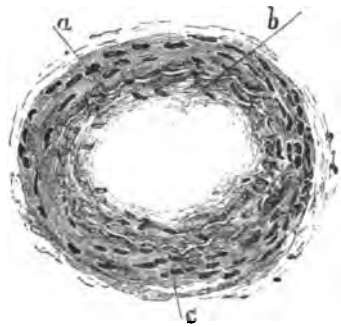

Fig. 24.—Renal arteriole, showing endarteritis obliterans. *a*, Swollen elastic lamina, its fibres separated and œdematous; *b*, Broad growth of connective tissue from the endothelial layer; *c*, Swollen muscular coat, with large distinct nuclei.

Convoluted tubules.—The tubules are in some places dilated, generally they are normal or undergoing diminution in size. They are sometimes filled with amorphous granular matter. In the least affected parts the epithelium is altered; it has lost its dark striated appearance and has become pale, the individual cells can be seen, the nuclei are quite distinct, but in some instances fail to take up staining fluids (*Fig.* 25). But for the most part the tubules are lined by a very flat nucleated epithelium, apparently the atrophied representative of the original cell layer (*Fig.* 27); the cavities of the tubes contain

Fig. 25.—Convoluted tubule, showing epithelium with distinct outlines, granular protoplasm and nuclei, which take on carmine staining well.

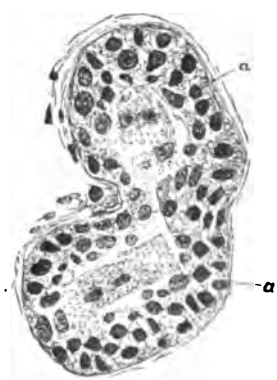

Fig. 26.—Convoluted tubule, with proliferated epithelium and casts in lumen.

rounded protoplasmic masses, nucleated cells, or colloid cast material (*Fig.* 26). Other tubules are denuded of epithelial lining. In other instances the tubules form cysts. This process is effected in a manner very like that already described in the Malpighian bodies. A cellular mass is formed in the

tube from the proliferation of the epithelium; this undergoes a retrogressive metamorphosis into gelatinous tissue and thence into simple colloid matter.

Fig. 27.—Dilated convoluted tubule, with atrophied epithelium: *a*, *a*, fragments of casts.

The basement membrane of the tubule becomes swollen and hyaline, and is lost in the new formation of connective tissue or becomes the wall of a cyst.

Straight tubules.—The epithelium is often proliferated; the lumina of the tubules are filled with colloid material mixed with cells. Other tubules are dilated and lined with atrophied epithelium. In the *medulla* many of the straight tubes are unaffected, but contain colloid matter (casts) in their cavities; others are dilated.

Acute nephritis is very prone to attack these kidneys at various stages of their evolution, so that their appearance is modified by the superaddition of the appearances of catarrhal nephritis. The kidneys vary in size, are paler, and under the microscope the epithelium is granular, vacuolated or fatty according to the duration of the process.

SYMPTOMS AND COURSE.—The beginnings of this disease are usually latent and obscure. Its symptoms are in many cases so little noticeable that patients continue to disregard them until some serious and too often fatal complication necessitates medical advice and leads to the discovery of grave

organic disease, which has advanced to its full development without any means having been taken to arrest it.

Even after a warning of this sort, there may be such a return of apparent health that all precautions are neglected, until a fresh attack proves fatal. A case will be quoted in which a single uræmic fit diagnosed correctly at the time was followed by eight years of apparent good health until a sudden attack of acute œdema of the lung proved fatal.

Such patients present themselves under the most varied semeiological conditions; they may complain of bronchitis or asthma, pain at the præcordia, palpitation or epistaxis, vomiting, diarrhœa, or hæmatemesis, giddiness, headache, affections of sight or hearing, or neuralgia; they may be attacked by apoplexies, convulsions, or coma; they may have articular gout, sciatica, lumbago or cramps; they may suffer from hæmaturia or symptoms of gravel or calculus; or they may chiefly complain of a skin affection—pruritus, eczema, erythema, purpura, etc.

Fortunately it is rare before forty years of age, but in patients after that time of life we must be for ever alive to the possibility of this condition underlying the complaint put forward. We can only escape falling into mistakes in practice by care, and the importance of making urinary examinations cannot be too strongly insisted upon.

Very frequently the patient comes first under observation owing to the supervention of an attack of acute catarrhal nephritis, by which the whole aspect of the case is temporarily altered.

The urine.—The characters of the urinary secretion are naturally the most important, unequivocal and significant of the symptoms of all forms of Bright's disease, nor are they less so in the present form, though the departures from the normal may not attract the patient's attention.

It is impossible to state precisely at what period in this insidious malady the urine shows signs of alteration, but it may be affirmed with certainty that no marked structural alterations can take place without evidence of them being discoverable in this secretion.

The *quantity* of urine, as in other forms of Bright's disease, undergoes alteration; but in this form it is not diminished in the early stages. On the contrary, when these cases come under observation the quantity is generally above the average, sometimes reaching or exceeding a hundred ounces in twenty-

four hours. But this increase, *as indicated by the necessity to rise at night to pass water*, is not always an early symptom. William S—— (Case 10, p. 130), who died six weeks after admission with advanced contracting kidneys, stated that he had only been disturbed at night for a week past. So, too, in the case of Cornelius H—— (Case 15, p. 138), this symptom had existed only three months, though he had all the other symptoms of an advanced case. On the other hand, Richard J—— (Case 23, p. 157), had been in the habit of getting up in the night to make water five or six times for the last ten years. But in all these cases its occurrence coincided with the development of the first symptoms which attracted the patient's attention. In a series of cases tabulated some years ago, the necessity to rise at night to pass water was present in seventy out of a hundred cases able to attend as out-patients.

It must be remembered that occasional rising at night for this purpose is common as a consequence of too free potations, of dyspepsia, and of excessive tobacco-smoking; while in local diseases of the bladder and neighbouring organs, it is often a marked symptom.

In the later stages the quantity of urine falls; this is due to failure of the heart, and even before irrecoverable collapse of the heart, the urine is liable to be diminished by its temporary weakness. In the case of George B—— (Case 21, p. 152) it is recorded that "he used to get up twice at night to make water and filled the vessel three parts full, but *since his illness this had passed off*." During the occurrence of an intercurrent attack of acute catarrhal nephritis the urine is diminished, and presents the usual character met with in primary acute attacks.

The *density* varies with the quantity, and particular samples passed during the day may be very much higher than the total quantity. In general it is below 1010. The *colour* is usually pale yellow, and the urine is *clear*, depositing only a very slight mucous cloud. The *reaction* is almost invariably acid, except when the patient is taking alkalies.

Bartels and Grainger Stewart state that the *urea* may not be diminished. This is true, as, for example, in the case of William S—— (Case 10), who, after living on milk diet for twenty days, passed 343 grains of urea in twenty-four hours. I have not felt justified in endeavouring to ascertain what maximum amount could be eliminated by these patients on

full diet. As a rule, however, they pass too little urea, that is, the daily output is under 300 grains,

The excretion of *uric acid* is stated by Frerichs to be lessened, especially towards the termination of the disease.

The *phosphates* are notably diminished; the *chlorides* are diminished, but become normal or in excess (LÉPINE) towards the end; the quantity of *sulphates* varies greatly, but is ordinarily low.

The *deposit*, as already stated, is scanty; it contains a few small hyaline and granular casts, but although not numerous they are very constantly present, and will be found if looked for in the proper way. In acute attacks the deposit is characteristic of acute nephritis.

Blood is not commonly present apart from acute attacks, bnt hæmaturia may occur, and is sometimes so profuse as to cause death from hæmorrhage (WEST).

Albumen is generally to be observed, if it is properly looked for. It may be absent in the night, but is present in the urine passed during the day, especially after breakfast. The explanation of the greater frequency with which I met with albumen amongst my out-patients is that I saw them in the morning, whereas in many places, notably in London, out-patients are seen in the afternoon; also that I always made my patients pass water for me at the time, and did not encourage them to bring it in bottles, as such urine is generally that passed the first thing on rising and has been secreted during the night.

Bartels has recorded a case which was kept under close observation until its termination, without the presence of albumen having been at any time detected.

The best method of testing for albumen is by boiling and acidulating with dilute acetic acid.

The quantity of albumen is small, in uncomplicated cases, but rises as the urine diminishes, following the law already established that albuminuria is increased by lowering the blood pressure. It is also increased in intercurrent attacks of acute nephritis.

Saliva.—This secretion has been found to contain urea (FLEISCHER) and albumen (SEMMOLA, VULPIAN, and STRAUSS) in certain cases.

The blood.—Anæmia is a marked symptom. Leichtenstern found the hæmoglobin co-efficient reduced from the normal 1330 to 802; Dickinson found the red corpuscles

reduced from the normal 5,000,000 to 3,921,875, and Rosenstein to 3,000,000. The water of the blood is increased from 784 parts *per mille* (CHRISTISON, OWEN REES, RAYER) to 821–853 parts *per mille*; while the albumen is diminished from 73·4 *per mille* to 68·5–59 *per mille* (OWEN REES, and RAYER); according to Lloyd-Jones the density of the blood is reduced in cases with gout to 1051, but in other cases it is normal, 1058. The urea is increased from the healthy standard of 0·016 to 0·084.

The heart.—The changes in the heart found *post mortem* in their order of frequency are: (1,) Hypertrophy, which is present in about 60 per cent.; (2,) Atheroma of the aorta, coronary arteries or endocardium, leading in the latter case to thickening of the valves without definitely impairing their functions; (3,) Valvular disease affecting in about equal proportions the aortic and mitral valves, stenosis of the latter valve being apparently much more common than simple dilatation; although this may be because it is so much more definite that the reporter has less difficulty in stating the fact; (4,) Fatty degeneration (granular atrophy) of the muscular fibre of the wall of the heart; (5,) Pericardial adhesions; (6,) Pericarditis. Pericardial effusion as part of general dropsy is not uncommon, but less so than pleural effusion.

The most definite sign of cardiac hypertrophy is displacement of the apex beat. This is normally in the fifth left intercostal space, well to the inner side of a line drawn vertically through the nipple. From my own observations, made on numerous out-patients, I am unable to accept the rigid descriptions that limit the normal position more than this. If the apex beat is in the nipple line or to the left of it, the heart is enlarged; still more manifestly is this the case if the impulse is in the sixth interspace, instead of the fifth. When there is much hypertrophy the impulse of the heart is often strong and diffused over a large area.

The first sound of the heart at the apex is commonly reduplicated, while the second sound in the aortic area is accentuated.

Johnson has suggested that the doubling of the first sound is due to the contraction of a dilated and hypertrophied auricle becoming audible, but the more generally accepted explanation is that of Sibson, who ascribed the reduplication to the asynchronous action of the two ventricles, due to the greater difficulty the left ventricle has in discharging its

contents owing to the increased pressure in the aortic system; while he explained the unity of the accentuated second sound by suggesting that the increased tension in the aorta allows it to complete the closure of its valves synchronously with the earlier filled but less actively distended pulmonary artery.

These changes in the heart sounds are very constant in contracting kidney, but their diagnostic value must not be over-estimated.

Doubling of the first sound may be heard in bronchitis and emphysema when there is obstruction to the discharge of the right ventricle, and in mitral constriction in cases where no murmur may be audible.

Accentuation of the aortic second sound is common in youths whose hearts under examination act with more than wonted energy. It may also be present wherever any local cause in the thorax (*e.g.*, tumour, aneurism) raises the blood pressure in the aorta.

But these changes in the heart sounds are so readily ascertained that they are of great value, as they often indicate the necessity for further careful investigation, and by attracting attention lead to the recognition of the renal condition which otherwise might pass unobserved.

Murmurs are not uncommon in contracting kidney. Systolic mitral murmurs may be due to dilatation or to the accidental association of old rheumatic endocarditis. According to Bartels acute endocarditis may occur as a result of renal disease. Aortic murmurs of obstruction or regurgitation, systolic and diastolic, are generally due to chronic endarteritis deformans attacking the aorta and spreading to the valves, but of course they sometimes have a rheumatic origin.

The presence of murmurs is an unfavourable element, as the heart has a very hard task to perform to compensate for the renal defect, and if handicapped by a valvular insufficiency it will probably fail early in the struggle.

From the point of view of the prognosis of *heart* disease, the supervention of kidney mischief is very unfavourable. A valvular defect, which was apparently compensated, will acquire fresh importance, and be followed by rapid heart failure and death.

Palpitation is a symptom commonly complained of. It is probably in many cases toxic in its origin.

The pulse.—The pulse rate in contracting kidney is generally high, from 90 to 100, but it may be normal, 70 to 80, or low,

60. In character it is usually hard, and incompressible, but varies in size, being sometimes full, more usually small. The hard radial artery, resembling the spermatic cord to the feel, is the typical high tension pulse of contracting kidney. But it is perhaps more commonly absent than present. When the artery is neither hard nor prominent the pulse will still be found to be incompressible, and even when this character is lost, the sphygmographic tracing may still show signs of peripheral obstruction to the circulation. (*Fig.* 28 illustrates a typical pulse tracing from contracting kidney.)

Fig. 28. Pulse tracing from case of R. J. Lithæmic kidney, chronic uræmia.

Ophthalmoscopic changes.—It is especially (if we exclude the nephritis of pregnancy the statement may be made more absolute) in this form of Bright's disease that we meet with affections of the retina. These have already been fully described (Chap. viii.); they consist for the most part of hæmorrhages, inflammatory exudations in and around the disc, and degenerative patches chiefly in the neighbourhood of the yellow spot. Sudden loss of vision may be due to hæmorrhage into the yellow spot.

CASE 9.—Frederick J——, aged sixty-three, attended as an out-patient on March 26, 1881, with pain in bowels, dyspnœa, cough and palpitation. He had been ill three months. He was in the habit of getting out of bed four or five times nightly to pass water. Heart irregular and intermittent. Urine albuminous. He returned on April 9th with loss of vision in the left eye and dimness of the sight of the right eye. Ophthalmoscopic examination showed: *Right eye,* H = ¼, disc very vascular; no exudations. *Left eye,* disc hazy, arteries very small, reduced almost to threads. Several large diffuse hæmorrhages *involved the whole region of the yellow spot.*

The following case is a typical example of albuminuric retinitis, and illustrates not only the various forms of retinal lesion, but the changes which may take place in them. As already explained, there is nothing essentially incurable in the retinal disease; its gravity depends upon its relation to advanced and incurable organic disease of the kidneys.

CASE 10*.—*Chronic lithæmic nephritis; albuminuric retinitis. Death. Autopsy.*

William S——, aged twenty-three, brass caster, admitted February 24th, 1888, complaining of headache, pain in the loins and dimness of sight. He

* Recorded by Mr. T. O. Crump, clinical clerk.

had been subject to headache for ten years, had often been giddy, but had not noticed any affection of his eyesight till a week ago, and for the last four days he had been vomiting. He had never had a fit, or been dropsical. He was a teetotaller, his work did not involve the use of lead, and he could remember no illness. His father died of dropsy and one sister of phthisis; his family history was otherwise unimportant. He had lately noticed that his eyelids were swollen in the morning and that his ankles had been œdematous on two occasions; he had been obliged to rise at night to pass water only for the last week. He was a well made man, with a yellow, waxy complexion, and some œdema of the lower eyelids. T. 98·4°. P. 90. R. 20. Tongue furred; bowels confined; liver and spleen normal. Lungs normal, with the exception of a few catarrhal sounds. Heart's apex in nipple line and fifth interspace; at apex reduplication of first sound; a systolic murmur in aortic area. Pulse incompressible, regular. Urine 30 oz.; sp. gr. 1010; acid, albuminous; urea 132 grains; granular, epithelial and hyaline casts, red and white blood corpuscles and renal epithelium in deposit. Ophthalmoscopic examination of right eye showed papillitis, with numerous radiating hæmorrhages along the course of the blood vessels; left eye, papillitis with several large round soft-edged white patches in the neighbourhood.

He went on pretty well for some time. On March 26th the eyes were examined and the right showed still swelling of disc with absorption of hæmorrhages; the left eye showed the outline of the disc well defined, the former rounded patches gone, but a fresh set of oval radiating bright patches on the inner side of the *macula lutea.*

On April 2nd he began to have headache. Temp. 99° F. He was put back on milk diet.

3rd.—Headache continued; partial unconsciousness; passed urine in bed; pupils sluggish to light. Temp. 98·4°.

4th.—Conscious. Temp. 98°.

5th.—Temp. 100° F. Face flushed; tongue dry; headache.

6th.—Temp. M. 100·8°. V. 102·r.

7th.—Temp. 101°. Unconscious; could not be got to take nourishment; breathing laboured; pulse very feeble; heart irregular and intermittent; death at 7.·5 p.m.

Date.	Quantity of urine in oz.	Quantity of urea in grains.	Quantity of albumen in grains.	Diet.
Feb. 26th ...	78	274·56	63	Milk
March 6th ...	72	316·8	60	„
„ 16th ...	78	343·2	117	„
„ 24th ...	66	261·36	60	Chicken or Fish
„ 31st ...	73	224·84	120	„ „
No urine collected after this date				

AUTOPSY. September 4th, 1888. Features pallid, nutrition visibly impaired; no œdema of legs, feet or scrotum.

Brain 47 oz.; hæmorrhage in patches over lateral aspect of right cerebral hemisphere; extensive hæmorrhage with red softening in the white

substance corresponding to the right temporo-sphenoidal and occipital lobes, the softened area surrounded by numerous miliary hæmorrhages into the white matter. The hippocampus and the postero-external edges of the optic thalamus on this side were destroyed; no hæmorrhage into the ventricle, but the hæmorrhage had oozed through the occipital lobe on to its outer aspect and spread over the whole of the cortex on the right side; serous effusions into the ventricles, the posterior part of the external capsule was involved; arteries at base of brain appeared normal.

Heart 15 oz.; no valvular lesions; coronary arteries good; great hypertrophy of left ventricle; wall measured $\frac{9}{10}$ in. thick. *Muscle* somewhat pale, but looked fairly normal. *Lungs* congested and œdematous, especially the inferior lobes. *Kidneys* barely 7 oz.; contracted, capsule adherent, surface granulated, but also somewhat hyperæmic; on section, the atrophy was more or less uniform; cortex of a mixed reddish grey and yellowish grey colour, and offered perceptible resistance to the knife edge.

Dropsy occurs in the acute forms, and has then the ordinary characters of the dropsy of acute nephritis. But in the commoner chronic form it only supervenes in the later stages as a consequence of heart failure, and then presents the usual character of cardiac dropsy, beginning in the depending parts, and gradually rising as the water gains on the pumping power of the heart.

DIAGNOSIS.—The latent nature of this disease has been referred to many times. It comes under so many disguises that it is only by possessing the conviction of its great frequency in persons over forty years of age that the physician will avoid overlooking many cases.

The hard pulse is one of the most accessible of signs, and is fairly constant, being present in 62 per cent. of my cases. Accentuation of the aortic second sound was present in 80 per cent.

Hypertrophy of the heart, indicated by displacement of the apex beat to the left of the vertical nipple line, was present in 60 per cent.; while a history of rising at night to make water was obtained in 70 per cent.

None of these signs taken singly is diagnostic, but they serve as guide posts to point out the way and lead up to the examination of the urine.

Albuminuria was present in 91 per cent. of my examinations, and will be very rarely found absent if the precaution be taken of obtaining a sample of the after-breakfast urine. It is worth remembering that a sample of the total mixed urine of the twenty-four hours, so desirable where quantitative analysis is required, is not the best for discovering a faint trace of albu-

men, owing to the greater portion of the urine, namely, that secreted at night, being often non-albuminous.

Casts are very constant and of great importance. I have found them in 88 per cent. of all examinations, but I do not think I have ever diagnosed contracting kidney until I had found casts, or ever failed to find them some time or another in every one of the cases of this disease which I have recognised during life.

The occurrence of retinal changes is too infrequent to be of great diagnostic value. Retinitis and neuro-retinitis appear to occur in only about 5 per cent., and small specks and hæmorrhages in 25 per cent.

Apart from their inconstancy they are not absolutely diagnostic when present. Typical albuminuric retinitis may be met with in anæmia; and diffuse neuro-retinitis, exactly like that of Bright's disease, has been seen associated with cerebral tumour. The specks are often extremely small and few in number, and are met with apart from Bright's disease. But combined with the other signs enumerated, these ophthalmoscopic appearances have great weight. In making a diagnosis all the symptoms should be passed in review.

Is it possible to differentiate between the two forms of chronic Bright's disease?—It is certain that, except in the case of typical gouty kidneys, it is difficult, if not impossible, to determine the etiology of the kidneys of chronic Bright's disease by their anatomical conditions; it is therefore not strange that the clinical diagnosis is not easy.

The following considerations may guide us: (1,) The age of the patient; the primary chronic form being very common after forty years of age. (2,) The presence of certain symptoms, such as polyuria, before the occurrence of an acute attack, although this might be represented as the commencement of the illness. (3,) The absence of dropsy or its presence only in depending parts. (4,) The presence of retinal changes.

PROGNOSIS.—There can be no doubt that this is an essentially incurable disease, and its course is liable to be interrupted by so many serious complications that the duration of life is always uncertain. Nevertheless, its normal evolution is slow.

Bright was aware that some cases last many years, and that this is possible even under unfavourable external conditions the following brief record shows.

CASE 11.—John P——, aged forty-eight, cabman, was in Hospital in 1877, with albuminuria and dropsy, under the late Dr. Russell. I examined his urine several times, and found it to contain numerous epithelial, hyaline and granular casts. This was probably an intercurrent acute attack. He attended for some time as an out-patient, and was then lost sight of. July 14th, 1881, he brought his son to see me, and I then took the following notes. J. P. gets up once every night to pass water. Urine pale, clear, 1010, no albumen or casts. Pulse distinct, but not hard. Aortic second sound accentuated. The disease seemed practically cured, but was only latent. On June 14th, 1884, he came up with diarrhœa, looking very ill. His urine was clear, pale, 1010, contained a good trace of albumen, a few granular casts, and blood corpuscles. Heart's apex not displaced; aortic second sound not accentuated. February 27th, 1887.—Gets up two or three times at night to pass water. Urine pale, clear, 1001, a faint haze of albumen. Has athetosis affecting the right hand and forearm.

In the month of February, 1888, I instituted an inquiry into the present condition of a few persons presenting symptoms of contracting kidney, whom I had rejected for life assurance some years back.

1.—T. B. D., male, aged thirty-eight; examined December, 1880; urine contained a trace of albumen with hyaline and epithelial casts. Reported to be *quite well.*

2.—R. T., male, aged forty-one; examined February, 1881; urine contained a trace of albumen, hyaline and granular casts. Reported to be *still alive and well.*

3.—J. H., male, aged fifty-eight, examined September, 1881; urine contained a faint trace of albumen, and a few hyaline casts. *Could not be traced.*

4.—C. R. G., male, aged sixty, examined November, 1882; urine contained a faint trace of albumen, but no casts. Died rather suddenly in the autumn of 1886.

The number is small, but it is noteworthy that there was only one death, and that that was a man at least sixty-five years of age when he died.

The most unfavourable symptom is *heart failure*, indicated by dropsy of the lower extremities, and diminution of the amount of urine. The presence of valvular disease, or any cardiac complication, is also most grave, on account of the dependence of the case upon the power of the heart to compensate for the renal defect.

Retinal disease is very unfavourable, because it rarely, if ever, occurs except in advanced cases.

Any of the symptoms of *uræmia* are bad, but life may be prolonged after many of them.

Dyspnœa is one of the most fatal of all the uræmic phenomena.

Acute *œdema of the lung* is always fatal.

The gravity of *acute intercurrent attacks* must be estimated by the amount of dropsy, just as in ordinary acute nephritis. The presence of cardiac complications is of course most unfavourable.

All *acute inflammatory* complications are very serious, especially pneumonia, pericarditis, and cellulitis, which are probably always fatal.

Any serious accident such as a *fracture* or condition requiring *surgical interference* usually terminates in death. Surgical statistics, especially of herniotomies in elderly people, are greatly prejudiced by this disease.

ILLUSTRATIVE CASES.

CASE 12.—*Sub-acute lithæmic nephritis in a case of heart disease. Death. Autopsy.*

F. I.——, male, forty-one, labourer, admitted April 8th, 1886, with shortness of breath. He had been quite well until Christmas, when he left off work owing to shortness of breath and cough. He attributes his illness to catching one cold after another. His urine has always been natural, and there has been no dropsy. He has been doing very heavy work and exposed to all kinds of weather.

When he was sixteen or seventeen years of age he had acute rheumatism, but can remember no other illness.

Father died suddenly of apoplexy. Mother died of bleeding from the nose. One brother died of a growth in the mouth (? epithelioma).

On admission his legs were swollen, but this disappeared rapidly after he was sent to bed. Tongue pale, moist, slightly furred; appetite bad; bowels regular. Liver dulness commences at sixth rib, and the edge can be felt two and a half inches below the costal border.

Spleen normal. Heart's apex in sixth interspace: a loud double murmur heard best in aortic area and conducted into the vessels of the neck.

Pulse collapsing, 108. Lungs resonant, breath sounds harsh and accompanied by numerous moist sounds.

Urine thirty-six oz., 1027; acid; deep yellow, turbid from urates; urea 2·2 per cent.; a faint cloud of albumen; hyaline casts; leucocytes and oxalates in deposit.

Progress of case.—He improved at first, but towards the end of April his cough became more troublesome. On May 2nd he had a severe attack of dyspnœa, his pulse became very weak, and he died at 1.50 a.m. on the following morning.

AUTOPSY, May 4th.—Well-made muscular subject; œdema of feet and ankles; slight general œdema of subcutaneous tissue.

Lungs very œdematous; about eight oz. of serum in each pleural cavity.

Heart, twenty-one oz.; right ventricle dilated and full of clot; pulmonary and tricuspid valves normal; left ventricle hypertrophied, walls thickened, cavity dilated, containing a small quantity of dark fluid blood; anterior cusp of aortic valve thickened and retracted; base of aorta irregularly dilated and the seat of extensive *endarteritis deformans*; mitral valve normal; muscular wall of heart pale and marbled; a patch of pericarditis on apex of heart with adherent organised lymph.

Liver, fifty-six oz.; a good example of cyanotic induration with atrophy; marked fatty infiltration in portal zones of lobules; consistence firm, rather leathery.

Kidneys, eleven and a half oz., cortex increased, pale, swollen and translucent in places, with brick red and yellowish mottling; capsules separated easily, leaving a pale marbled surface (red and greyish yellow).

On microscopical examination the convoluted tubes were generally dilated, in some the epithelium was swollen, granular, vacuolated and fatty; in others it was atrophied or reduced to a narrow border of protoplasm. Except where degenerative changes were present the nuclei stained well. The glomeruli were hypertrophied, the capillary loops appeared cloudy and indistinct and showed an increase of nuclei. They were not congested as a rule. Here and there small stellar patches of interstitial change were met with. In the pyramids the capillaries were considerably engorged.

CASE 13.—*Chronic lithæmic nephritis; chronic endocarditis; heart failure. Death. Autopsy.*

Thomas S.——, aged forty, gardener, admitted March 28th, 1886, with cough, tightness of the chest, weakness and swelling of the legs.

A month ago he noticed his eyelids and hands were puffy, and he made very little water; then his legs swelled; and a fortnight ago he took to his bed.

He could remember no previous serious illness; he had never had dropsy or any trouble with his water before; he had never had gout, or acute rheumatism, but had often had rheumatic pains in his knees and shoulders, and had been confined to the house for a fortnight with them. For the last six months he had been rising at night to pass water.

His home and circumstances were comfortable, but his work exposed him to cold and damp, and he was in the habit of drinking four or five pints of "sweet ale" daily.

His family history was unimportant; father died aged seventy-two; mother died aged seventy-six. Seven brothers and sisters alive and well; only one had died in infancy.

He was a well-built and well-nourished man, with a ruddy complexion; there was œdema of the conjunctivæ, lower extremities and scrotum. T. 97·5°; P. 90; R. 20; tongue furred in centre, red at edges; bad taste in mouth; appetite good; very thirsty; bowels confined; abdomen distended; some ascites; hepatic and splenic dulness normal.

Heart's apex in fifth interspace, inside the vertical nipple line; no murmur; no accentuation of aortic second sound. Pulse regular, not hard.

Breath sounds harsh, with moist râles posteriorly. Vision good; ophthalmoscopic appearances normal.

Urine 28 oz.; sp. gr. 1022; acid; urea 217 grains *pro die*; albumen 71 grains *pro die*; epithelial, fatty, hyaline and granular casts, blood corpuscles and blood casts, with renal epithelium in the deposit.

He did not improve under treatment; he had profuse diarrhœa, and on April 7th he was in a very serious condition. In the evening he complained of feeling very weak; he became cyanosed, and died at 9.20 a.m.

AUTOPSY, April 9th, 1888.—Extensive general anasarca; head and face congested; *rigor mortis* passing off.

Thorax.—About a pint of clear fluid in each pleural cavity. *Lungs.*—Congested and œdematous. *Heart* weighed 17 oz.; pericardial sac contained about 2 oz. of fluid; right side of heart full of clot; tricuspid and pulmonary valves healthy; mitral cusps thickened, shortened and yellow, with small, firmly adherent vegetations on their auricular surfaces; aortic valve incompetent; segments glued together, thickened, stiff and calcareous in places. Under the microscope the heart fibres showed a little "brown atrophy," but were not fatty.

Abdomen.—Liver 79 oz., fatty. *Spleen* 6 oz., soft, pale. *Kidneys* together weighed 17 oz., greatly swollen, mottled red, white and yellow (roan). On section, the cortex was of the same colour; the Malpighian bodies were very distinct, and some showed the waxy reaction with iodine. The consistence of the organs was soft and friable.

Under the microscope the following changes were noted:—*Malpighian bodies*, the capsules were broadened and nucleated (*pericapsulitis*), and the lining epithelium proliferated (*endocapsulitis*); the glomerular tufts were covered with nuclei, and one had completely undergone hyaline change. *Blood vessels* dilated; there was hypertrophy of the muscular wall, with proliferation of the endothelium of the intima (*endarteritis obliterans*). *Connective tissue;* this was generally broadened out and full of round brightly stained cells. The great exception was the capsule of the kidney, which did not appear thickened. *Epithelium;* the tubes were everywhere lined with fatty epithelium; it was difficult to find one that was not so, even in the medulla. There was no appearance of proliferation of epithelium, though some tubes were filled with *debris*, in which some small rounded nucleus-like bodies could be seen.

CASE 14.—*Acute attack supervening in the course of chronic lithæmic nephritis. Recovery.*

Michael H——, aged thirty, iron worker, admitted April 4th, 1888, with headache, tightness of chest, and swelling of face and legs. He had scarlatina when a child, but enjoyed good health till eighteen months ago; since then he had suffered from severe headache and bronchitis. At Christmas he caught cold, and his legs swelled, but this passed off. Three weeks ago he noticed that his water was smoky. He admitted having been a heavy drinker, and his work exposed him to severe changes of temperature. His mother died of asthma. He was a fairly well nourished man, with a flushed face; when examined the œdema of the legs had passed off from rest in bed. T. 98·5°; P. 72; R. 83; tongue clean; appetite good; bowels regular; liver dulness three and a half inches in the vertical nipple line; some dulness in flanks, which changed with his position.

Heart's apex in sixth intercostal space, one and a half inches to the left of the nipple line. At apex, first sound reduplicated; in aortic area,

second sound accentuated. Pulse was hard and incompressible. Lungs normal.

Urine 56 oz.; sp. gr. 1017; acid; straw colour, smoky; white deposit; urea 344 grains; albumen 377 grains; deposit contained a few epithelial and numerous hyaline and granular casts, with red and white blood corpuscles and renal epithelium.

With rest in bed and diaphoresis he improved rapidly.

April 14th.—There was no trace of ascites. Urine 60 oz.; sp. gr. 1022.

18th.—Urine 62 oz.; sp. gr. 1010; very little blood; albumen 528 grains; granular and hyaline casts with blood corpuscles and renal epithelium.

There was continued improvement.

May 1st.—Urine 60 oz.; sp. gr. 1006; straw colour; albumen 396 grains.

3rd.—Allowed to get up. Urine 62 oz.; sp. gr. 1020; albumen 327 grains.

8th.—Urine 60 oz.; sp. gr. 1015; straw colour; urea 448 grains; albumen 316 grains; a trace of blood with guaiacum and ozonic ether; a few hyaline and granular casts, blood corpuscles and renal epithelium in the slight white deposit.

10th.—He was made an out-patient.

After April 11th he had milk diet with chicken or fish.

CASE 15*.—*Chronic lithæmic nephritis; albuminuric retinitis; uræmic dyspnœa.*

Cornelius H——, aged fifty-eight, admitted on June 12th, 1888, with severe frontal headache made worse by lying down, cough, and dyspnœa, frequent micturition, especially at night, partial loss of sight and swelling of the feet towards night.

He had been ill six weeks, and worse for seven days. He was sent to me from the Eye Hospital, where he had complained of headache and dimness of sight, and was suffering from nasal catarrh with congestion of the conjunctivæ. Albuminuric retinitis was recognised there, so he was transferred to me.

His father died of bronchitis, aged fifty-six; mother died aged seventy, cause unknown. Three sisters died between thirty and forty, cause unknown. He has had three children, of whom two died in infancy; the third is living, aged twenty-five, and is strong and well.

Patient had worked as a match maker all his life. He denied having been intemperate; his only drink had been half a pint of beer at supper three or four times a week. He had a good home, but his workshop was close. He could remember no illness, except "congestion of the kidney" eight years before. On enquiry about the congestion of the kidney, he said that he passed blood in his water and was delirious, and that he was ill in bed four weeks. There had been no return of hæmaturia. He denied ever having had gout.

He was a very old-looking man for his years, with a very puckered, wrinkled face, scanty hair; skin of face and conjunctivæ slightly jaundiced; expression of face dull and apathetic. There was slight œdema of the legs and feet. Temp. 98°.

Lips cyanosed; teeth very defective; tongue clean; mouth very dry;

* Recorded by Mr. F. H. Nootl, Clinical Clerk.

appetite good ; great thirst ; bowels confined ; no ascites ; liver dulness four inches in vertical mammillary line. Heart's apex a little external to the vertical mammillary line in the fifth left interspace ; sounds pure ; aortic second sound accentuated. Pulse full, cord-like, incompressible, 96.

Respirations hurried, 48 ; a little cough ; no expectoration ; breath sounds and percussion note normal. There is persistent dyspnœa.

Ophthalmoscopic appearances.—Right eye.—One or two small hæmorrhages below the disc, and a number of small round patches of atrophic retinitis on the outer side. *Left eye.*—No hæmorrhages, but a larger group of the same patches on outer side of disc.

Urine.—Slight uneasiness in loins ; water passed six or seven times during the night for three months past ; 66 oz. ; sp. gr. 1010 ; pale, acid ; a dense cloud of albumen ; urea ·9 per cent. (260 grains) ; under microscope numerous leucocytes and a few hyaline and granular casts.

He complained of being unable to sleep in the hospital, and insisted on going out five days after admission.

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CHAPTER XII.

OBSTRUCTIVE NEPHRITIS.

(SYN. SURGICAL KIDNEY; PUERPERAL KIDNEY; ASCENDING NEPHRITIS.)

INFLAMMATION of the kidney which arises in the course of many affections of the pelvic organs has close pathological relationships with what is generally known as Bright's disease. A description of it will make clearer the general doctrine of the broad unity in type of the anatomical changes met with in all cases of nephritis, and it will add an additional argument to the proof of the efficiency of the renal lesion in the production of the cardio-vascular changes.

ETIOLOGY.—The causes of this form of nephritis are to be sought in some obstruction to the outflow of the renal secretion. It is identical in its simpler form with nephritis produced by ligature of the ureter (STRAUSS and GERMONT), but this primary condition is apt to be complicated by an acute infective process, starting from inflammation or traumatism in the urinary passages, *e.g.*, cystitis, catheterism. The most common causes are enlarged prostate, stricture and cystitis, uterine and ovarian tumours, pregnancy, pelvic inflammation (pyo-salpinx), tubercle and tumours of the bladder, and procidentia uteri; their degree of frequency being in something like the order given. As in other forms of chronic nephritis, cold may easily set up acute intercurrent attacks.

Sex.—My figures give a much larger proportion of males than females, in the ratio of seven to one. The females include the following cases: procidentia uteri, one; hysterectomy for uterine fibroma, one; removal of appendages for double pyo-salpinx, one; ovariotomy, one. But as the number of cases of special diseases of women treated at the General Hospital is very small, while the proportion in which this lesion is found is large, there is reason to think that the disease is more common in females than the above figures would suggest.

Age.—In accordance with the nature of the causes the disease is much more common after middle life.

MORBID ANATOMY.—The kidneys are usually above normal size, rarely small. The capsule is generally thickened and more or less adherent; the surface is granular, red in colour or more often pale. On section, the organ is often tough, soft and flabby. The cortex is sometimes swollen, often reduced in width; the pelvis is always dilated and contains purulent urine, while its mucous membrane is congested and œdematous. Patches of opaque greyish infiltration are visible invading the medulla and cortex, and hæmorrhagic streaks and spots are often present. When there is tubercular disease of the bladder, tubercles may be found in the kidneys. Both organs do not always present identical appearances. One may look fairly normal and the other be in an advanced state of disease, or one may be enlarged, pale and fatty, while the other is smaller, red and granular; Crooke has described a case in which one kidney only was diseased, the cause being compression of the corresponding ureter. Collections of pus may be found in the cellular tissue around the kidneys. In recent cases, especially in connection with pregnancy, the kidneys may appear only swollen and hyperæmic.

The microscopic appearances are as follow :—

Glomeruli.—Some appear normal; others have their nuclei increased, while others again are in a state of hyaline degeneration. Blood may be found extravasated in the intra-capsular space.

Blood vessels.—In advanced cases the larger vessels show well-marked *endarteritis obliterans* with hypertrophy of their middle and outer coats. The capillaries of the cortex are dilated and full of blood; others, especially those in the boundary zone, may have their walls thickened.

Convoluted tubules.—These are generally of normal size. The epithelium is in parts normal; in others it shows the appearances of catarrhal nephritis. Some of the tubules are filled with leucocytes, which infiltrate the basement membrane.

Straight tubules.—In the medulla many of these are widely dilated, to a less extent in the cortex, and they often contain colloid material (casts). The epithelial lining is in places being pushed off by invading leucocytes, which may fill up the lumen of the tube.

Connective tissue.—This is swollen and hyaline. Here and there areas may be seen so thickly crowded with invading

leucocytes that the normal structure of the kidney is quite hidden, and in places veritable abscesses are visible. This description is based upon cases complicated by more or less acute interstitial nephritis, set up by cystitis; it is probable that where there is simple obstruction there is no interstitial nucleation (STRAUSS and GERMONT).

Angus Macdonald, in his description of the kidney of eclampsia, found only dilated tubules, with altered epithelium and colloid masses in their cavities. This is no doubt the early stage of the uncomplicated process. If not interfered with and given a persisting cause, *e.g.*, enlarged prostate, it ultimately eventuates in red contracting kidneys, such as are described in the following notes from the pathological register :—

CASE 16.—*Enlarged prostate; cystitis; surgical kidneys.*

H. C.———, admitted August 3rd; died August 17th. NECROPSY, August 18th, 1886. A spare, emaciated subject.

Heart 9½ oz.; large milk spot on right ventricle; aorta and coronary arteries atheromatous; right ventricle enlarged; slight chronic endocarditis of mitral valve; muscle dark, a little fibrous in places.

Lungs.—Lower lobes congested and œdematous; upper lobes emphysematous; general bronchitis. The base of the left lung was deeply congested and the pleura was slightly inflamed.

Liver 52 oz.: capsule a little opaque and thickened; parenchyma pale, fatty and mottled with congestion.

Kidneys 8½ oz.; capsules adherent; *red granular kidneys;* pelves dilated with purulent urine; on the left side the cellular tissue round the lower end of the kidney was infiltrated with pus; ureters dilated near their entrance to the bladder.

Bladder.—Great hypertrophy of walls; mucous membrane much inflamed and discoloured, showing small ulcerated elevations to which phosphatic deposit was adherent; prostate much enlarged, fibrous and indurated; prostatic and membranous urethra showed signs of chronic inflammation.

SYMPTOMS AND COURSE.—These cases generally come under medical or surgical observation on account of the local trouble which causes the kidney mischief, for in this, as in the red contracting kidney of dyscrasial origin, the symptoms are latent, while any special urinary symptoms are masked by the local disorder. The disease usually becomes noticeable when acute nephritis has supervened, and this brings with it corresponding changes in the clinical phenomena.

The urine.—In pronounced chronic cases the urine is increased in amount to 80 or 100 oz.; it is of low density, generally acid unless it has undergone decomposition, usually turbid from some amount of cystitis being present, and con-

taining a moderate amount of albumen, with a little blood. The deposit is muco-purulent, containing hyaline and granular casts, epithelium, pus cells, blood corpuscles, and often triple phosphates and micro-organisms. When acute nephritis has supervened the urine is diminished, the amount of albumen and blood is increased, the density is higher, and epithelial and blood casts are found in addition to the other elements in the deposit. In the former case the *urea* may be normal in amount, but in the latter it is greatly reduced.

The heart is hypertrophied in a considerable proportion; out of twenty-seven cases it weighed over 10 oz. in twelve, and the left ventricle is described as hypertrophied in one that weighed 10 oz., which may, therefore, be fairly included; thirteen out of twenty-seven are very nearly 50 per cent. This is confirmed by other observers: in enlarged prostate it was observed in four out of ten cases (JEAN); in other cases in five out of twelve (WEIL); while Féré has noticed its frequent occurrence in the bodies of females with procidentia uteri.

Dropsy is generally absent or only slight, but when acute nephritis occurs or heart failure sets in, dropsy supervenes just as it does in lithæmic kidney.

Uræmia.—In pregnancy uræmic convulsions are common, probably because, as already pointed out, there are other co-operating factors present to produce a dyscrasia. Apart from this condition classical uræmia is not common. The usual form is the typhoid type, with dry tongue and feeble pulse. It is a form in which septicæmia plays an important part. Senator has described the type resembling "diabetic coma" as frequently occurring in cystitis (*Vide* Chapter VII., p. 62).

DIAGNOSIS.—These cases can only be diagnosed when their etiology is thoroughly grasped, and the symptoms looked for carefully in cases where the disease is likely to be present.

Evidences of high arterial tension may be found in the character of the pulse, in the accentuation of the aortic second sound and the doubling of the first sound at the heart's apex. Displacement of the latter outwards indicates cardiac hypertrophy. The urine should be collected for twenty-four hours, its quantity measured, its solids and especially its urea quantitatively estimated, and casts looked for.

PROGNOSIS.—Where the disease is due to pressure only, uncomplicated by cystitis, a good result may be hoped for,

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provided the obstruction is removable and is not of too long duration. This is exactly the condition in most cases due to pregnancy, hence the satisfactory recoveries so often seen after parturition has taken place. In most other cases the cause is of such persistence that the prognosis is very bad.

ILLUSTRATIVE CASES.

CASE 17.—*Enlarged prostate; cystitis; ascending nephritis.*

A. B., thirty-five, furnace-man, admitted Oct. 23rd, 1888, complaining of swelling of the legs and face, and pain in the back.

His present illness had lasted only a week; he thought he had caught cold, as his work is very hot, and he was in a draught. The next morning his water was scanty and dark red, and has remained diminished in quantity ever since.

Five years ago he was in the hospital with a similar attack, also brought on by cold. He was ill a month. He could recollect no other illness; he had never had gonorrhœa or gout. He had never had any difficulty or pain in making water or had an instrument passed, or was aware of having any bladder disease. General surroundings at home comfortable; had plenty of good food; drank three pints of beer daily, and at one time more than this. Family history good.

Present condition.—Patient is a well-developed, well-nourished man, with a rather sallow complexion. His face looks puffy, but there is no œdema of the eyelids. There is no œdema of the legs or scrotum, but he has been twenty-four hours in bed. T. 97·5°; R. 24; P. 60. Tongue clean at tip, furred posteriorly; teeth defective; gums sore; breath foul; appetite pretty fair; no discomfort, bad taste, or flatulence after food; bowels regular before admission, but not opened since.

Vertical liver dulness 4¼ inches, reaching just below the costal border. Spleen not enlarged. No ascites. Chest well formed; respiration vesicular; percussion note normal. Heart's apex in fifth interspace inside vertical nipple line; first sound feeble at apex; second sound loudly accentuated in the aortic area. Pulse 60, full, not easily compressible.

No headache, giddiness, or affection of special sense except slight deafness. Complains of his two forefingers being "dead and white" with the cold in the mornings. No loss of muscular power or common sensibility.

Ophthalmoscopic appearances negative.

Urine, 24 oz., reddish brown, turbid, faintly alkaline; sp. gr. 1015; urea 1·6 per cent.; loaded with albumen; contains blood and peptone, no sugar; white heavy deposit, which under the microscope appears to be composed of pus cells, and flask-shaped or spherical colonies of micro-organisms enclosed in the capsule.

Some urine was drawn off with a catheter under antiseptic precautions, which was sent to Dr. Crooke, who reported as follows: "Urine acid, straw-coloured, tinged with blood; muco-purulent deposit; urea 1·1 per cent.; albumen 1 per cent.; no sugar; blood; pus; no casts; zoogloea masses of bacteria and micrococci, of which several varieties are present."

Some nutrient gelatine was inoculated with the urine and sent to Prof. Crookshank.

It was noticed that although the bladder was full of water when the catheter was introduced, the patient had had no desire to micturate. The lateral lobes of the prostate were moderately enlarged.

Oct. 28th.—Mr. Barling examined the bladder with the cystoscope, and reported as follows: "Direct cystoscope passed without difficulty; bladder previously washed out and about six to seven oz. of fluid injected. Medium rather turbid, but not bloody. Mucous membrane on trigone and immediate neighbourhood elevated, œdematous and fluffy on surface. Neither ureteral orifice could be seen. Still further back the changes were the same, but less marked. No ulceration was seen. The ordinary distribution of vessels on the mucous membrane was quite obscured." The urine remained in the same state.

On Nov. 1st the bladder was ordered to be washed out with boracic lotion daily.

Nov. 6th.—The bladder has been washed out daily since it was ordered. The urine is now pale greenish yellow, turbid, acid, depositing three-quarters of an inch of pus, containing a trace of blood. Under the microscope the flask-shaped and spherical encapsulated masses are much less numerous, but there are plenty of irregular zooglœa masses. Complains of epigastric pain; tongue furred and brown. Has had flatulence. He has been taking saccharin.

As washing out the bladder seemed to be followed by an increase in the amount of pus it was stopped on the 10th, when the amount of pus at once fell to half, but since then it has varied a good deal.

His legs began to get very œdematous, and this remained in spite of his being kept in bed, and of the large amount of water he was passing, which averaged over 80 oz. daily.

The following is the urine report for Nov. 25th; Urine 88 oz., acid, straw-colour, blood-tinged; sp. gr. 1012; deposits muco-pus; urea ·9 per cent.; albumen ·9 per cent.; blood and pus present; slight acetone reaction; one or two flask and hour-glass shaped colonies enclosed within a membranous envelope; also diffuse distribution of bacilli and mycelium-like threads; some hyaline masses to which large fatty cells adhere as if portions of large hyaline or colloid casts (DR. CROOKE).

He left the Hospital *in statu quo.*

CASE 18.* *Cystitis; bronchitis; ascending nephritis; septicæmia.*

Martha L———, aged forty-three, housewife, admitted May 26th, 1886, with swelling of legs, shortness of breath on exertion, and cough.

She had had pleurisy ten years ago, but no other illness. There was nothing to be made out of the family history. Her surroundings at home were comfortable; she had been temperate, taking only one half-pint of beer daily at her supper. A strongly built, well-nourished woman; her skin had a slightly yellow tinge, but her conjunctivæ were white. There was slight œdema of the legs. T. 98·6°; P. 66. Tongue furred; appetite poor; complained of thirst, of flatulence after food, and of vomiting before admission; bowels confined; abdomen distended; vertical liver dulness one and a half inches in the nipple line; ascites. Heart's apex just inside vertical nipple line, in the fifth interspace; there was a diastolic murmur best heard to the left of the apex beat. Pulse full, regular. Urine 10 oz.; sp. gr. 1017; acid; straw yellow colour, smoky;

* Recorded by Mr. F. H. Noott, Clinical Clerk.

deposit reddish brown; urea 83·6 grains; deposit contained epithelial, hyaline and granular casts, red and white blood corpuscles and renal epithelium.

June 1st.—The cardiac murmur had disappeared, and was never heard again. Urine 30 oz.; Temp. 99·6°; P. 68.

3rd.—Vomiting; urine 44 oz.; Temp. 102·6°.

4th.—Vomiting continued, the patient was pale and sweating profusely; her tongue was dry; lungs normal; urine had to be drawn off with catheter, 28 oz.; sp. gr. 1026; acid; claret colour; reddish brown deposit; urea 147·84 grains; albumen quarter column; deposit contained blood corpuscles, pus cells, epithelial, granular and hyaline casts, and renal and vesical epithelium. Evening temp. 104° F. P. 84.

5th.—Still vomiting; hæmaturia persisting; no pain. Temp. 101·6°; Urine 42 oz.

6th.—Still vomiting; sputa blood-stained; impaired resonance at right apex, with a few rhonchi and râles audible. The patient was becoming distinctly more emaciated and anæmic. Urine 34 oz. Temp. 100°.

8th.—Blood examined with the hæmocytometer appeared normal. Urine 44 oz. Temp. 99·4°; P. 72; R. 48.

9th.—Better. Urine 34 oz. Temp. 98°.

10th.—Not so well. Urine 36 oz. Temp. 97°.

11th.—Better. Urine 40 oz. Temp. 97·2°.

12th.—Passed urine without the catheter. There was pain and swelling over the right parotid, causing inability to open the mouth, but fluids were readily swallowed; there was no redness of the skin; tongue dry; bowels confined. Temp. 98·6°. Urine 60 oz.; alkaline; sp. gr. 1012; slightly blood-tinged; whitish viscid deposit; urea 475·2 grains; a cloud of albumen; deposit contained no casts, but red and white blood corpuscles, pus cells, mucous corpuscles, vesical epithelium, with crystals of triple phosphate and urate of ammonia.

13th.—Swelling great, skin over it hot and red. Urine 58 oz. Temp. 104·4°.

14th.—Swelling less, mouth could be opened more freely; breath foul. Urine 40 oz. Temp. 98·4°.

15th.—Swelling going down; vomiting recurred. Urine 38 oz. Temp. 97·2°.

16th.—Vomiting stopped; catheter required again; swelling still less. Urine 40 oz. Temp. 98°.

17th.—Very slight swelling left; no vomiting; a few râles at left apex; no cardiac murmur; catheter still required. Urine 32 oz.; sp. gr. 1013; alkaline; smoky colour; muco-purulent deposit; urea 239 grains; albumen one-twelfth column; deposit contained no casts, but pus cells, blood corpuscles, vesical epithelium and triple phosphates. Temp. 97·6°.

18th.—Patient looked very ill, and complained of pain in the bowels, nausea and severe diarrhœa. Pulse 160, very feeble; retention of urine; pain ceased in the course of the day. Temp. 96·8°. Urine 14 oz.

19th.—She had passed a fair night, but the diarrhœa persisted. Temp. 96·8°; P. 132, very feeble. She vomited, and the ejected matter contained 0·5 per cent. of urea. In the course of the day the diarrhœa stopped, and she complained of no pain. Evening temperature 96·2°. Urine 10 oz. She died the following morning at 6.25 a.m.

NECROPSY.—*Lungs, right*; œdema and hypostatic congestion of inferior lobe; diffuse bronchitis and muco-pus in the bronchi. *Left;*

pleuritic adhesions of the base to the thoracic wall; inferior lobe congested and somewhat collapsed. *Heart* 9 oz.; no valve lesions; left ventricular wall hypertrophied. *Liver* 50 oz., mis-shapen; right lobe much flattened out, its upper surface grooved by the ribs, and its inferior border reaching nearly to the umbilicus. *Spleen* 5 oz., normal. *Kidneys* 7 oz.; capsules stripped well; surface greyish red; stellate veins prominent. On section, several abscesses were found in the cortex of the right kidney; the surrounding substance seemed infiltrated and of an opaque grey reddish mottled appearance, as though it were the seat of an acute interstitial nephritis. *Right ureter* dilated; mucous surface bathed with semi-purulent urine. *Bladder*; walls thickened, much dark spotty ecchymosis of the mucous membrane, which was swollen, injected and infiltrated *Intestines* collapsed; wall of small intestine intensely injected; ileo-cæcal valve very œdematous.

TREATMENT.—The *indicatio causalis* is to remove the obstruction, and when this is recent, as in pregnancy, a cure usually results. The propriety of inducing labour must depend upon the urgency of the symptoms. But in most other cases the propriety of operative proceedings is open to grave problem, as they are so uniformly fatal. In determining this difficult question much must depend upon the nature of the obstruction, and also upon the urgency of the local symptoms which the operation is designed to remove. If there are any reasonable grounds for thinking the obstruction has existed not more than a year the chances of a favourable result are improved.

When ascending nephritis is present the use of catheters is attended with great danger, for this is the condition in which the so-called "catheter fever" is likely to be induced.

The general management and treatment of these cases should be conducted on the lines laid down in the previous chapter.

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CHAPTER XIII.

THE COMPLICATIONS OF CHRONIC BRIGHT'S DISEASE.

THE complications of chronic Bright's disease are so numerous and important that they require a chapter to themselves.

An analysis of a hundred cases of chronic Bright's disease, taken from the pathological registers of the General Hospital, gives the following as the morbid appearances met with :—

	NATURE OF LESION.	NUMBER.
Brain ...	Congestion	2
	Meningitis	3
	Œdema	7
	Hæmorrhage	8
Lungs ...	Pleuritic adhesion	10
	„ effusion	17
	Congestion and œdema	56
	Bronchitis	6
	Emphysema	7
	Infarcts	2
	Phthisis	7
	Pneumonia	19
	Œdema of glottis	1
Heart ...	Pericardial adhesion	4
	„ effusion	9
	Pericarditis	1
	Fatty heart	7
	Thickening of valves	16
	Hypertrophy	60
	Mitral stenosis	9
	„ incompetence	1
	Aortic „	9
	Aneurism of aorta	2
	Atheroma of aorta or coronary arteries	30
Liver ...	Fatty infiltration	29
	Cirrhosis	13
	Lardaceous degeneration	2
	Nutmeg liver	6
	Atrophy	3
	Cancer	2
	Hydatid	1
	Abscess	1

NATURE OF LESION.		NUMBER.
Spleen ...	Gall-stones	6
	Capsule thickened	2
	Infarcts	2
Peritonæum	Ascites	2
	Peritonitis	9
	Thickening	1
Stomach ...	Catarrh	2
Intestine ...	Tubercular ulcers	1
	Dysenteric „	1
Skin ...	Cellulitis	4
	Purpura	3
	Eczema	1

URÆMIA.—The most important complications are those classed together under this convenient name. Uræmic vomiting and convulsions are common in the acute febrile nephritis of children, but are not of very serious significance. In the chronic form they are always grave, yet temporary recovery may take place under the most unfavourable circumstances.

Skin eruptions occur sometimes. Rosenstein has described one resembling measles; *erysipelas* and *erythema* are common. *Eczema* sometimes occurs.

CASE 19.*—*Hæmorrhagic exfoliative dermatitis. Death. Autopsy; Chronic lithæmic nephritis.*

Ann D——, aged sixty-four, admitted December 13th, 1886, with an eruption all over her body. She said that three weeks previously brown patches appeared on her face and arms, which all at once became scaly and peeled off "like shavings," the scales being renewed. The rash spread over her body, and in the second week blisters formed, chiefly on her hands, which broke and became red and sore; her nose bled, and blood came from her mouth; the gums were very sore; her water was bloody, and her motions dark, and there was a discharge from both her ears.

She had had no previous eruption; when a child she had acute rheumatism. No history of syphilis.

She could give no details of her family history, except that her father and mother died young, she thought of "fever," and that her only sister was alive and well.

On admission her face was covered with crusts and dried blood. There was blood on her gums and tongue, and under the latter were small ulcers. Her whole body was covered with a hæmorrhagic eruption of spots as large as a pin's head; in places these had coalesced to form larger patches. There were numerous blisters the size of threepenny pieces on the arms, which were covered with scaly scabs. In the flexures of the elbows, knees, groins, and axillæ, as well as on the shoulders and

* Case recorded by Dr. Stacey Wilson, House Physician.

buttocks, the skin had lost its epidermis and bled freely. A very offensive smell arose from the patient. The following day the whole of the epidermis from the sides and soles of the feet came away, leaving raw bleeding surfaces. On the 16th, the third day after admission, she rapidly sank and died.

AUTOPSY, December 17th.—*External appearances.*—A well nourished woman, with well marked *post mortem* rigidity and hypostatic congestion. The entire body was to a greater or less extent marked with either small round deeply stained hæmorrhagic spots, or large irregular red patches of denuded epidermis, or actual ulceration. On the face was a mixture of spots, of varying size and depth of colour, and small red patches. The mucous membrane of the gums was rough and irregular, but no hæmorrhages could be seen. The spots were most abundant on the shins, calves and abdomen; the patches most on the buttocks, backs of hands and feet, flexures of elbows and knees, groins and vulva.

Brain.—Basilar artery atheromatous; dilatation of vessels of pons and medulla; otherwise normal.

Lungs.—Slightly adherent; some hæmorrhages on the diaphragmatic pleura, the largest the size of a sixpenny piece.

Heart.—Several small hæmorrhages in cellular tissue at roots of great vessels outside epicardium; weight 11 oz.; much fat on surface; muscular wall soft and thin. Valves healthy, except a little atheroma on the mitral valve. No sub-endocardial hæmorrhage. Aorta dilated and slightly atheromatous.

Liver 46 oz.; soft, congested and fatty.

Gall-bladder dilated, adherent to transverse colon; contained two white mulberry calculi, and 1½ oz. of dark thick bile.

Kidneys 9 oz.; capsules adherent; surfaces granular; cortices narrow and hard.

Spleen 2 oz.; normal.

Intestines.—There was a hæmorrhage the size of a shilling in the wall of the ascending colon, about three inches above the cæcum, and in the mesentery there was a small cyst containing ½ oz. of clear fluid. The *psoas and iliacus* muscles on both sides contained hæmorrhages, more on the right side. No other hæmorrhages were observed in any situation.

Dr. Le Cronier Lancaster has drawn attention to the gravity of this eruption, which he describes as commencing by simple macules, and passing through the stages of papules, pustules, and multiple abscesses to diffuse exfoliation or vesication of the epidermis; it is often hæmorrhagic, and usually occurs only a few weeks before death.

Dr. Pye-Smith recognises (1,) a simple erythema, occurring chiefly on the trunk, and not attended by sweating; (2,) a dark red papular rash, seated on a dry, rough, scaly surface, chiefly seen on the outer surfaces of the limbs and shoulders; (3,) a moist dermatitis affecting the neck, arms, and legs; (4,) universal exfoliative dermatitis, apparently identical with the case just recorded.

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Hyperæsthesia of the skin, snatching and burning sensations are occasionally present.

The peculiar condition called "*dead fingers*," is considered by Dieulafoy to be a uræmic symptom, but this is probably an error; it certainly occurs in persons in perfect health.

Deposits of crystals of urea on the skin have been noticed by many trustworthy observers, amongst others by Bartels.

Symmetrical gangrene has been observed in uræmia by Debove.

Vomiting and *diarrhœa* are evidently caused by the vicarious elimination of urinary constituents by the gastro-intestinal mucous membrane, chiefly urea, which is transformed into carbonate of ammonia. It is also probable that the vomiting is often cerebral. In children, vomiting, evidently uræmic and probably cerebral, is very common in acute nephritis.

Hiccough may be very persistent, as in the following case, where it was relieved by the simple method of irritating the anterior nares with a rolled-up piece of blotting paper, suggested by Dr. G. A. Gibson.

CASE 20.*—*Uræmia; hiccough; peculiar dropsy; peculiar albumen.*

Joseph B——, aged thirty-five, slater, was admitted into the General Hospital on November 20th, 1886, complaining of swelling of the face, sickness and headache. About five years ago he first had attacks of sickness and headache, with sharp pains in the left loin and in the groins, not shooting down the leg or into the testicle, but apparently in the course of the colon; he was an in-patient in this hospital at that time, and again in the spring of the present year. On the latter occasion there was no œdema; his chief troubles were headache and vomiting. Since his discharge his face has swollen occasionally; two weeks ago he was very sick and giddy, and in a similar attack he was admitted.

On admission the swelling of his eyelids was so great that he could hardly see out of them. The skin of his face was swollen; no œdema elsewhere. He was a well-developed and fairly well-nourished man.

Pulse 96, hard, full and regular; R. 16; T. 95·4°. Tongue large, pale, and indented at edges. No pain after food; vomiting at times; bowels regular; liver and spleen normal; no ascites.

Heart's apex in fifth intercostal space inside nipple line; a faint systolic murmur with first sound at apex; aortic second sound louder than pulmonary.

Lungs resonant; breath and voice sounds normal.

No pain or difficulty in micturition; urine 30 oz.; acid; sp. gr. 1012; pale straw colour; very slight deposit; urea 1 per cent.; albumen quarter column; no blood; hyaline, granular and epithelial casts, leucocytes and squamous epithelium.

* Recorded by Mr. Pogson, Clinical Clerk.

Nov. 22nd.—Eyelids more swollen and red, looking as if he had erysipelas.

Nov. 23rd.—Vomited at 8.30 a.m. Œdema of eylids *quite pink* from injection, but less in amount.

Nov. 27th.—Œdema of eyelids less; vomiting again.

Nov. 29th.—Not so well; *much troubled with hiccough.*

Dec. 2nd.—Swelling of face less. Frequent vomiting.

Dec. 3rd.—No sleep last night. Frequent vomiting. *Hiccough, removed by irritating nostrils with a rolled-up piece of blotting paper.*

Dec. 6th.—Vomiting still. A uræmic fit at 3 a.m.; another at 3.45, in which he died.

When in hospital previously his urine on one occasion presented the following characters :—

April 13th, 1886.—Urine 70 oz.; sp. gr. 1018; alkaline. On boiling and adding acetic acid there was a faint haze. On boiling and adding nitric acid there was no change. On adding a good deal of nitric acid and then boiling there was a haze. On adding nitric acid in the cold there was a dense precipitate. With Esbach's solution the quantity was estimated at 0·1 per cent.

Dyspnœa occurs in uræmia in various forms. Howard enumerates the following :—

1. Continuous dyspnœa.
2. Paroxysmal dyspnœa.
3. Both types alternating.
4. Cheyne-Stokes breathing.

But to these we may add a form described by Lecorché as *Laryngeal*, in which the respiration is noisy and sibilant as in croup, attributed by him to spasm of the laryngeal muscles; and the type described in the case of Harriet B., in which the breathing is slow and deep. The most characteristic form is that usually called uræmic asthma, which may be continuous or paroxysmal, as stated by Howard. The patient sits up in bed struggling for breath as in true asthma.

Numerous cases of Cheyne-Stokes breathing have been observed; in one instance, reported by West, the condition persisted for three months; one by Brush lasted three weeks; and another by Brush recovered after six days.

CASE 21. — *Chronic lithæmic nephritis; Cheyne-Stokes breathing; recovery.*

George B——, aged fifty-nine, railway servant, was admitted into the General Hospital on June 4th, 1886, complaining of shortness of breathing and swelling of his legs.

His present illness began three months ago with pains in his side, and his feet and legs swelled a bit. This passed off in a week or two, but came on again and lasted till the present time. His previous health had been good; he had never had rheumatism, rheumatic fever or gout. His father and mother died at advanced ages, and all his brothers and sisters are alive and in good health.

He was always fond of beer, drinking four or five pints daily, but he was obliged to keep sober on account of his work. He used to get up twice at night to make water, and filled the vessel three parts full, but since his illness this had passed off.

Patient was a well-developed, ill-nourished man; face ruddy; conjunctivæ muddy; some œdema and cyanosis of skin of legs; abdomen distended, measuring thirty-seven and a half inches at umbilicus. P. 90; R. 22; T. 98·2°. Tongue clean; appetite good; no discomfort after food; no vomiting; bowels not open, but have been regular; liver enlarged, measuring nine inches of vertical dulness in mammillary line; spleen not enlarged; some ascites. Slight cough, watery mucous expectoration; dulness, deficient vocal fremitus and breath sounds at both bases, more on the right side, with exaggerated breathing above the level of dulness. Heart's apex diffused, but extending to sixth interspace; a loud systolic murmur at apex; pulmonary second sound accentuated.

No difficulty or pain in micturition; quantity 16 oz.; sp. gr. 1020; deep orange colour; slight cloudy deposit; acid; faint trace of albumen; no sugar; no blood; hyaline and fatty epithelial casts, leucocytes and oxalates.

June 5th at 11 p.m., well-marked Cheyne-Stokes breathing; average length of pause 20½ seconds; varying from fifteen to twenty-five seconds; out of nine observations, in six it was twenty seconds; active respiration lasted on an average 37½ seconds; in six out of nine observations it was thirty-five seconds, in which period there were about twenty-three respirations. The pulse got slower towards the end of the pause, and beats fuller during descent of respiration.

June 10th.—Had a fairly quiet night, but two bad attacks of dyspnœa after getting out of bed to micturate.

June 11th.—10 p.m. worse; weaker; Cheyne-Stokes breathing less marked.

June 13th.—Abdomen tapped and 64 oz. drawn off.

June 16th.—Cheyne-Stokes breathing again; pause lasted fifteen to twenty seconds; respiratory activity forty to forty-five seconds.

June 20th.—Had an attack of dyspnœa last night.

After this he improved and was discharged on July 16th.

Giddiness.—This is a very common symptom, and is often the first one to be complained of. It is very alarming, and as it is generally persistent it is not easily tolerated, though the patient usually at first attributes it to some temporary "biliousness." It differs, however, from stomach giddiness in being relieved by lying down.

Headache.—The characteristic headache of uræmia is occipital, but it is sometimes frontal. I have not observed any special connection, such as Bartels recognised, between migraine and Bright's disease.

Uræmic deafness has been described by Dieulafoy, and cases have been recorded by Rayer, Rosenstein, Dommergues, Gurowitsch, Lecorché, Eichhorst and Downie. The last

observer suggests that it is due to minute hæmorrhages in the cochlea, but it is much more probable that the auditory centre like the visual centre is paralysed by the poison.

Uræmic blindness is a purely cerebral phenomenon without any definite ophthalmoscopic changes. The loss of sight may be complete or incomplete; it is usually transient, lasting from twenty-four to thirty-six hours, but Förster has described a case which lasted seventeen days and terminated in recovery.

Hemiopia sometimes occurs.

Transient hemiplegia without palpable localised lesion is not very uncommon, and cases have been recorded by Paetsch and von Jaeckel. It lasts usually about twenty-four hours; it is as a rule incomplete; the reflexes are abolished or diminished; it may be followed by contractures; the face may be affected; ptosis is exceptional; conjugate deviation of the eyes has been observed; aphasia may coincide with right hemiplegia; hemianæsthesia is usually present, and the anæsthesia may affect the organs of special sense. It is of grave prognosis (BOINET).

Delirium is not a very common complication. It is often preceded by headache, visual disturbance and mental confusion, and is generally quiet, but Wagner has recorded a case in which each convulsive attack was followed by violent mania with a temperature of 107·4°.

Scholz has described a form of chronic delirium, characterised by hallucinations of sight, delusions of persecutions, convulsions and vomiting without headache.

Haslund has published a case of furious delirium with hallucinations which lasted four months. The patient was tormented by hallucinations, and his voracity and salacity were extreme. He died collapsed.

Lecorché and Talamon give a case of a maniac in whom the delirium came on with the disappearance of polyuria and ceased as that returned.

Raymond has described cases of mental disease dependent upon chronic nephritis, and he has been supported by other examples published by Barie, Dieulafoy and Tuttle.

Amnesia with loss of words has been described by Brieger; the case recovered after some time.

CASE 22.—*Chronic nephritis. Uræmic delirium. Death. Autopsy.* George R——, aged eighteen, was admitted into the General Hospital

on October 6th, 1886, complaining of frontal headache, sickness, loss of appetite, and making a lot of water at night.

He said he did not feel weak, and did not think he had lost flesh. Four months ago his illness began with eight fits, extending over two nights and a day. He had had no fits before or since. He had never had any illness or accident, except having his head cut open by a swing-boat eight years ago. He had never had dropsy, any swelling, scarlatina, or gonorrhœa.

He was a badly-nourished, ill-developed, sallow-faced lad. P. 100, small, weak, regular; T. 98·8°; R. 24. No œdema.

Chest symmetrically formed; expansion equal; percussion note resonant; breath sounds, vocal fremitus and resonance normal.

Heart's apex in fifth interspace inside the nipple line; impulse variable; action regular; no thrill; sounds at apex normal; in tricuspid and pulmonary areas there was a systolic blowing murmur; the aortic second sound was accentuated; there was no murmur in the neck.

Tongue flabby, indented at edges, pale, but clean; bowels regular; no discomfort after food; appetite poor. Liver and spleen normal; no pain or difficulty in making water, but gets out of bed every half hour to make it; quantity 54 oz.; sp. gr. 1012; alkaline; greenish yellow; deposits white flocculent precipitate; urea ·8 per cent.; albumen half column; no sugar or blood. Under the microscope groups of leucocytes, hyaline and granular casts, red blood corpuscles, squamous and renal epithelium, triple phosphates, granular *débris* and masses of micrococci were detected.

He complained of dimness of vision, which had come on for twelve or thirteen weeks, being only able to read large capitals. With the ophthalmoscope extensive neuro-retinitis was seen in both eyes, with large white glistening patches of retinal atrophy; both eyes were equally bad.

Oct. 6th.—Complained of fixed pain in the left side; bowels confined; tongue foul.

7th.—Vomited about two pints of brownish watery matter, free from blood; bowels acted loosely; tongue very brown. Complained of sick headache all last evening.

9th.—In the afternoon was restless, thirsty and faint. He vomited a good deal, and was given some brandy, after which he improved.

10th.—Had a sleepless night, but was quiet; complained of headache and chilliness; vomited five times during the night, 15 oz. in all, which contained 0·15 per cent. of urea.

11th.—*Has been whistling and singing most of the night;* slept only half an hour; kicked the clothes off continually; complains still of headache. Vomiting again this morning.

12th.—Slept only from 12 to 12.30 a.m.; *restless, noisy, and delirious;* he continued delirious all day, and towards evening got out of bed; he slept with a chloral and bromide draught. To-day, some dulness, friction, deficient breathing, and coarse crepitation were noticed over right side of chest anteriorly. His temperature continued to be normal or subnormal. Pulse 120; respirations 36 to 48. He died the following day at 1.15 p.m. without any development of fresh symptoms.

AUTOPSY, October 14th.—*External appearances.*—Features pale; lips bluish; *rigor mortis* present; hypostasis more marked posteriorly.

Head.—No trace of previous injury to skull; brain congested; excess of serous fluid in sub-arachnoid space and ventricles; no gross lesion in any part of brain substance.

Heart.—Pericardial cavity contained 4 oz. serous fluid; heart 13 oz.; generally hypertrophied, especially left ventricle; muscular wall firm and rigid; valves normal.

Lungs both adherent by old fibrous adhesions; old caseous and fibroid phthisis at left apex. In centre of right middle lobe was a small hard nodule, composed of caseous material, surrounded by a capsule of pigmented fibrous tissue, while a similar, but rather larger nodule was in the upper lobe of the same lung. The bronchial glands were enlarged, caseous and encapsuled in fibrous tissue; the left lung contained several smaller caseous nodules of the same kind.

Liver 51 oz.; pale, soft and fatty. *Spleen* 5 oz.

Kidneys, right, 5½ oz., enlarged, surface greyish red mottled with yellow spots; capsule slightly adherent; cortex increased, swollen, greyish with yellow mottling and hyperæmia intermingled, translucent-looking in places and generally fatty; medullary cones congested, almost claret-coloured; *left*, 4 oz., smaller, more granular, capsule more adherent.

Among the minor phenomena of threatening uræmia, *Cramps* are common. Charcot has seen a kind of *tremor* resembling paralysis agitans, and Jaccoud has described *tonic spasm* of the flexors of the forearm and the posterior muscles of the neck.

Headache is a very common prodromal symptom; it may be frontal or occipital, but the latter is more characteristic.

Twitchings are also a common early symptom, and these are closely related to *convulsions*, which may attack single groups of muscles, and to Jacksonian epilepsy, or convulsions without loss of consciousness, which may be unilateral (TENNESON and CHANTEMESSE).

Convulsions of the epileptic type constitute the common uræmic fit, they are accompanied by total loss of consciousness, biting the tongue, and foaming at the mouth, and are generally followed by deep coma. The attack may consist of a single paroxysm or a succession of these, the patient lying unconscious in the intervals, breathing stertorously, or in a sort of deep sleep from which he may be partially roused. Brissaud and Larring have described a case followed by catalepsy.

Coma may be the result of a convulsive attack, or may come on gradually, or suddenly as in apoplexy. Roberts has given several cases of this sudden onset.

The *temperature* during the attack is generally subnormal. Roberts has recorded a case in which the temperature fell as low as 94·4° F., and Hirtz another in which it fell to 93·9°,

while Bourneville has published temperatures as low as 93·1°, 91·1°, 89·6°, and even 86·1°. According to Hutinel these low temperatures are more often met with in those forms of nephritis following diseases of the urinary passages, *e.g.*, surgical kidney, and Netter observed a temperature of 86° in a case of anuria due to purulent nephritis with a twist of the left ureter.

MacBride gives the following conditions as those under which lowering of the temperature is always present: (1,) In kidney diseases following affections of the urinary passages with complete obstruction; (2,) In uræmia in old persons; (3,) In uræmia occurring in old standing kidney diseases complicated by vomiting, diarrhœa and hæmorrhages; (4,) In uræmia which supervenes in cancerous cachexia and marasmus.

In other cases elevation of temperature has been observed even as high as 105·8° and 107·4°, but this has always been followed by a rapid fall (RICHARDIÈRE, GILLET). Lépine found that a high temperature could be induced in animals by ligaturing the ureters and connecting them above the ligatures with a reservoir of salt and water under sufficient pressure to drive back the urine into the circulation. This result is singularly at variance with the above noted clinical observations.

Carr has recorded a case of recovery after an attack of febrile uræmia.

The *pulse* is generally quick, but may be as low as 60 or even 40.

CASE 23.—*Chronic lithæmic nephritis; uræmic coma. Recovery.*

Richard J——, aged forty, brewer, was admitted into the General Hospital on March 20th, 1886, complaining of swelling, which began in his legs, not in his face, and at the same time he noticed that his urine was smoky and diminished in quantity. His previous health had been good; he had never had scarlatina or gout; he was ridden over about two years ago and got "concussion of the spine," for which he was an inpatient in the surgical wards of this hospital. He was not told that his kidneys were hurt.

He had been in the habit of getting out of bed to make water five or six times for the last ten years; he drank about three pints of beer daily, but no spirits as a rule.

He was a stout, well-developed man, with general anasarca, but no fluid in pleuræ or peritonæum. Pulse 84, regular, full; R. 24; T. 98° F.

Tongue clean; fulness after food; bowels loose from purgatives; liver normal; spleen a little enlarged.

Heart's apex in fifth interspace in nipple line; systolic murmur at apex, not constant; aortic second sound accentuated.

Lungs resonant; breath and voice sounds normal.

Urine 44 oz., acid; sp. gr. 1015; smoky, yellow; white deposit; urea 1 per cent.; albumen five-sixths column; blood present; peptones present; fatty, hyaline and epithelial casts; white and red blood corpuscles and renal epithelium.

He complained of dimness of sight; there were subconjunctival hæmorrhages in the right eye. With the ophthalmoscope numerous atrophic patches were seen in both retinæ, and a recent hæmorrhage in the right eye; the outlines of both discs were gone, the arteries were very small, and the veins large.

In spite of purging and diuretics his dropsy increased, and his urea excretion was very little. On March 26th it was 174 grains per diem. He began to complain much of occipital headache and pain behind his eyes.

April 4th.—His legs were drained.

5th.—He began to be drowsy, and passed a stool under him. He continued in this apathetic condition, passing urine and fæces in bed till his tongue grew dry, sordes appeared on his teeth; he was *delirious* and did not seem to recognise people. This continued till April 25th, when he gradually sank into coma. When seen his pupils did not react to light; he could be partially roused; he had vomited several times. The coma seemed to deepen, and an ineffectual attempt was made to bleed him. He was ordered a hot-air bath, in which he sweated freely, and next morning was better. After this he slowly improved, and after being for a time at the Jaffray Hospital, was discharged, free from œdema and fairly well, but quite blind.

HÆMORRHAGES of all kinds are very common. Profuse hæmaturia has been already alluded to, but hæmorrhage may take place from the bronchial or intestinal mucous surfaces, into the retina, the tympanum and the skin, while probably it constitutes the most common cause of cerebral apoplexy. The cause of the hæmorrhage is in all cases the same,—degeneration of the small vessels and increased blood pressure.

CASE 24.—*Chronic lithæmic nephritis; pneumonia; cerebral hæmorrhage. Death. Autopsy.*

Edward C——, aged thirty-two, foreman at bicycle works; admitted April 9th, 1886, with headache, shivering and pains in the back, worse on the right side and increased on deep inspiration. He had been ill one day.

Except vague complaints of rheumatism, without joint affection, there was no previous illness. His habits were temperate and his home comfortable, but his work exposed him to changes of temperature. He was a well-built and well-nourished man, but looked ill; his face was dusky, and he complained of feeling cold. T. 104°; R. 38; P. 120.

There was no cough, and no abnormal physical signs could be detected. There was no œdema. Tongue dry in centre.

Urine 24 oz.; sp. gr. 1013; acid; copious brown deposit; albumen ·1 per cent.; epithelial, hyaline, and blood casts, with blood corpuscles, and renal epithelium in the deposit.

The next day he began to vomit, and his bowels became loose, but the stools were dark. His evening temperature was 103° F. On the 13th he was delirious, and enteric fever was suspected, but there was no rash, and the stools were not at all characteristic. On the 16th dulness and coarse crepitation were made out at the right base posteriorly, and on the 17th his temperature came down to normal, and remained down afterwards. He was some time getting better. The urine continued to be bloody and albuminous, but sufficient in quantity. On May 22nd the urine report is as follows; 56 oz.; sp. gr. 1010; acid; pale straw colour; urea ·95 per cent.; albumen ·5 per cent.; a trace of blood; epithelial and hyaline casts, with blood corpuscles, and renal epithelium in the flocculent deposit.

On June 8th he was made an out-patient. He was re-admitted on September 29th with effusion in the pleural cavity. On October 6th œdema was for the first time noted in the legs; this increased, and never left him. His urine contained albumen, and numerous epithelial and hyaline casts, blood and epithelium. He was very noisy and restless for some days, but by October 11th he was quieter. On the 17th pericardial friction was heard. He began to vomit and complained of headache on the 21st. Ascites was noted on the 27th. He remained more than two months in the Hospital, but insisted on going out on December 9th. His legs were still a little œdematous and there was fluid in the peritonæum; the urine was fairly abundant, 52 oz.; slightly albuminous, but in the last examination no casts were seen; urea 1·05 per cent.

He was again admitted on January 8th with great swelling of the abdomen, legs and scrotum. Urine 68 oz.; sp. gr. 1012; pale brown colour; slight white deposit; a quarter column of albumen; a little blood, and no casts. In the morning of January 18th he vomited again, and at 7.40 p.m. when seen he appeared to be in a fit affecting the left side; the left eyelid drooped, and the left arm was rigid, with occasional spasmodic jerkings; he could not speak, but made intelligible signs with his right hand. His teeth were clenched, and now and then ground firmly together. His breathing was noisy and occasionally stertorous. Vomiting came on, and he died at 9.20 the same evening.

AUTOPSY, January 19th, 1887.—Body of a fairly nourished man, *rigor mortis* and *post mortem* staining well marked. Legs and feet œdematous, abdomen greatly distended with a large quantity of clear straw-coloured serum. Pericardium containing from 1 to 2 oz. of blood-stained fluid; there was also a small quantity of lymph on the surface of the heart and serous surface of the pericardium.

Heart 1 lb., hypertrophied, wall of left ventricle ¾ in. thick, muscle substance hard, firm and pale. Cavities not dilated. Musculi papillares and columnæ carneæ well developed; aortic and pulmonary valves normal; mitral orifice admitted three fingers; tricuspid, only the tips of five fingers; the posterior cusp of mitral valve shortened but not thickened.

Lungs.—Left pleura contained a large quantity of clear straw-coloured fluid; the parietal pleura was much thickened, and the lung bound down to the spine by firm adhesions, the lower lobe was entirely collapsed and attached to the diaphragm by a short tough fibrinous band about the thickness of the little finger. The upper lobe was crepitant throughout, but much firmer than normal. The whole lung weighed 8½ oz., and had somewhat the appearance of a Florence flask, the lower lobe forming the neck.

Right lung 1 lb. 4 oz. ; this was adherent, specially the lower lobe, the surface of the lung being torn in removing it ; the tissue was firm and congested.

Liver 3 lbs. 2 oz. *Spleen* 4½ oz. *Kidneys*, right, 4 oz. ; left, 3½ oz., they were small and pale, and on section were found to be hard and fibrous, cutting grittily, the cortex narrowed, of a pale yellowish white colour, hard and fibrous ; the pyramids were pale, also hard and fibrous, the capsule thickened and adherent, on removing it the surface was mammillated.

Bladder was empty and contracted, nothing abnormal was noticed.

On removing the *brain* the convolutions on the (left?) side were flattened, the (left?) lateral ventricle was much distended with blood and clots, and some blood had found its way into the ventricle on the other side, the corpus striatum and optic thalamus were much lacerated and disorganised by the hæmorrhage.

CHRONIC PACHYMENINGITIS.—I take the following from the report of the *post mortem* examination of a man named J. C——, in the Pathological Register of the General Hospital.

Brain.—Dura mater adherent to the calvarium and in part to the surface of the brain ; the meninges were generally thickened all over the vertex, œdematous, and the *pia mater* was here and there adherent to the vertex, the grey matter of which appeared dull, cloudy and mottled with yellow. There was much serous effusion in the sub-arachnoid space and ventricles. A small "psammoma" was found adherent to the membranes behind the left crus. The under surface of the left temporo-sphenoidal lobe was broken down with red and yellow softening ; the corpora striata and optic thalami were cloudy and mottled yellow and pinkish grey. In the softened area the small vessels showed with the microscope fatty degeneration of their walls. *Heart* 13 oz. ; left ventricle considerably hypertrophied ; no valve lesion. *Kidneys* 9 oz. ; atrophied, capsules adherent ; surfaces granular ; cortices visibly diminished and fibroid.

HEART FAILURE.—This is a very common occurrence in the later stages. It is usually indicated by rapid dilatation of the heart, and there is often pallor, dyspnœa on exertion, or dropsy of the lower extremities. I have met with several examples of *infective endocarditis* occurring in association with Bright's disease, and in one instance there was extreme *hæmorrhagic myocarditis* with recent endocarditis affecting the mitral valve.

ŒDEMA OF THE GLOTTIS.—This is a well-known complication of general dropsy in acute and sub-acute nephritis, but it is not commonly known to occur in chronic Bright's disease.

A man was brought into the hospital dead or dying, and on *post mortem* examination there was well marked œdema of the glottis, without general œdema. He had typical contracting kidneys ; his heart weighed 13½ oz., its valves were thickened, and the coronary arteries atheromatous ; his lungs

were congested and œdematous; his liver was cirrhotic and his brain œdematous.

The *larynx* is not uncommonly the seat of acute or chronic catarrh.

CONGESTION AND ŒDEMA OF LUNGS.—Among the most common *post mortem* appearances in persons dying with contracting kidney, whatever the cause of death may have been, are congestion and œdema of the lungs. This is the condition which during life probably gives rise to the symptoms of bronchitis which are so common in these patients. Many elderly patients who complain of "bronchitis," and who have cough and difficulty of breathing, will be found on examination to have no physical signs sufficient to account for their complaint. If the case is gone into and the urine examined sufficient evidence will often be found to enable it to be recognised as a latent example of contracting kidney.

One of the fatal complications which may arise in the course of latent contracting kidneys is *acute œdema of the lungs*. Its explanation is not at all clear, but it is generally attributed in a loose sort of way to the dyscrasia. This is all very well if there is dropsy elsewhere, but is no sort of explanation for the sudden development of dropsy in the lungs when all the rest of the body is free. Acute œdema of the lungs is too rare a condition to have attracted much attention. Standard text books either leave it out altogether or refer to the unimportant forms accompanying pneumonia and bronchitis, or to the pulmonary œdema of mitral disease.

In seeking an explanation for it we must apply the principles laid down in the chapter on Dropsy. Gradual heart failure would not give rise to these sudden attacks of œdema. They are not like the creeping dropsy of failing heart, but resemble the outburst of anasarca in acute nephritis. We must look therefore to some causes favouring the rapid outpouring of lymph. These may perhaps be found in hypertrophy of the right side of the heart and in increased permeability of the capillaries due to some local poison, possibly such as Wooldridge found favoured œdema.

In the case about to be related œdema of the lungs followed an anginal attack, in which the pulse was not affected. Could the angina have been due to some affection of the right side of the heart? Could there be spasm of the pulmonary vessels giving rise to heart pain, and followed by paralytic distension and œdema? These are possibilities.

CASE 25.—*Chronic lithæmic nephritis; uræmia; death from œdema of lung.*

A lady, aged sixty, of gouty antecedents, eight years before had had an epileptiform seizure, recognised at the time to be "uræmic." No other kidney symptoms had developed, except the necessity to rise at night to pass water. For the last few weeks there had been a little dry cough, with some dyspnœa on exertion, and a complaint of pain in the chest.

One day, after a short walk, she was seized with a violent attack of pain at mid-sternum, which went through to her back and down the left arm to the *thumb*.

When seen by me at 2.30 p.m. her face was pale and anxious, extremities cold. The heart's apex was in the sixth left interspace, an inch outside the vertical mammillary line; the sounds were very feeble. The pulse was full, soft and regular, but she had been inhaling nitrite of amyl. Respiration was easy; slight cough; no expectoration; breath sounds normal. She complained a good deal of the pain, which was not relieved by any remedy. By 4.30, when I left her, her face was less anxious, her hands were warmer, and her pulse was still full and quite soft. She continued better and sat up a little during the afternoon, but about eight o'clock difficulty of breathing commenced. When I returned at 9.30 there was marked œdema of both lungs, moist bubbling râles could be heard all over the chest and she presented cyanosis of the face, cold clammy skin, etc.

All remedies were useless; she gradually became unconscious, and died at 11.30. No urine was passed after the first onset in the middle of the day, when, at the same time the bowels were moved. The pulse remained full till quite near the end.

BRONCHITIS accompanied by emphysema is found *post mortem* with some frequency, but, as already hinted, not so frequently as the cough and dyspnœa from which these patients suffer would suggest.

CASE 26.—*Chronic lithæmic nephritis; gout; bronchitis; eczema; uræmic delirium. Death. Autopsy.*

James W——, aged sixty-five, upholsterer, admitted January 10th, 1888, with cough, dyspnœa on exertion, and a breaking out on his skin.

He had had a cough all the winter, but the eruption came out eight weeks ago. Twenty years before he had a slight attack of acute rheumatism, he was ill only a week; five years ago he had an attack of gout, and for some winters past he had suffered from bronchitis. He had lately been badly off for food, but he had taken one to two pints of beer daily.

He was a well-developed, poorly-nourished man; the skin of his head, face, and forearms was intensely red, and covered with crusts; he complained a great deal of burning and itching. T. 100°; P. 96; R. 24. Tongue furred; bowels confined. Heart sounds feeble, but no murmur; pulse weak and compressible. Breath sounds feeble anteriorly; posteriorly, harsh and accompanied by moist râles.

Urine 50 oz.; sp. gr. 1026; contained a trace of albumen; uratic deposit.

After admission he made no improvement.

January 23rd.—T. 100°; P. 96; R. 42. He had been delirious, getting out of bed and asking where he was; urine 50 oz.; sp. gr. 1022; urea 407 grains; a thick cloud of albumen; a trace of blood; hyaline and granular casts.

27th.—T. 102·8°; P. 102; R. 36. Still delirious and getting out of bed.

28th.—T. 101°; P. 108; R. 50. Quieter; towards evening increased difficulty of breathing.

29th.—Had passed a bad night with his breathing; his respirations were sighing and laboured; expiration was greatly prolonged. T. 102°; P. 90; R. 34.

31st.—Pain, redness and swelling over right hip joint. T. 100·5°; P. 100; R. 48.

February 1st.—Breathing noisy from rhonchi; hip very red and swollen. T. 102·5°; P. 98; R. 46.

2nd.—Towards evening breathing very soft. T. 102°; P. 100; R. 52. Urine 28 oz.; sp. gr. 1020; acid, straw colour, smoky; white flocculent precipitate; very thick cloud of albumen; deposit contained cellular hyaline and epithelial casts, blood corpuscles and blood casts, and renal epithelium.

3rd.—Breath very short; hip much inflamed. Death at 2.50 p.m.

AUTOPSY, February 4th, 1888.—*Abstract of notes:*—There was a large abscess above the hip joint, connected with dead bone. The lungs showed chronic bronchitis and emphysema, with dilated bronchi. The pericardium was adherent, and the heart hypertrophied, weight 15 oz. The kidneys were typical red granular atrophic kidneys, weight 8 oz. The arteries in the boundary zone were thickened and patent. There were numerous yellow spots in the cortex, which were composed of urate of soda. In the metatarso-phalangeal joints of both great toes there was chronic arthritis, with deposit of urate of soda in the fibrous tissues.

PNEUMONIA.—It is very common to find contracting kidneys in the bodies of persons dying of acute lobar pneumonia; eighteen out of a hundred cases of chronic Bright's disease collected for statistical purposes had this association. No doubt the presence of such a condition is a most unfavourable element in the prognosis of acute pneumonia. Lobular pneumonia may occur in connection with bronchitis, and hypostatic pneumonia may supervene in the later stages of slowly dying cases.

CASE 27*. *Bronchitis; chronic lithæmic nephritis; lobular pneumonia. Death. Autopsy.*

J. J——, male, sixty-seven, chaff-cutter, admitted September 20th, 1886, with cough and shortness of breath.

Family history unimportant. Had rheumatic fever twenty-four years ago, and has since suffered frequently from rheumatism, colds and cough. Admits that he has not been always temperate, and has frequently been insufficiently fed. Three weeks ago he caught cold, but getting worse, and a sharp pain attacking his left side, he came to the Hospital.

* Recorded by Dr. Lewis Hawkes, Acting House Physician.

A decrepit old man, lame from rheumatic stiffness of the hip; face pale; conjunctivæ jaundiced; respiration laboured. T. 100°. Lips blue; no teeth; tongue pale, moist, furred at sides; appetite bad; constant thirst; throat dry and parched. Has pain after food; eructations of wind; water brash; bowels confined. Liver projects an inch below ribs. Inguinal hernia on right side. Heart sounds reduplicated in pulmonary and tricuspid areas; apex beat not to be felt, but dulness does not extend outside nipple line. Sputa frothy; cough troublesome; respirations 30; breathing harsh, expiration prolonged, accompanied by musical rhonchi all over chest. Gets up several times at night to make water.

Urine 20 oz.; acid; sp. gr. 1015; deep amber, smoky; white flocculent precipitate; faint cloud of albumen; blood present; no sugar; under microscope hyaline casts, a few red blood corpuscles and leucocytes, free renal epithelium, spheroidal and polymorphous epithelium from urinary tract, squamous epithelium, spermatozoa, and uric acid.

Progress of Case.—The cyanosis increased; he was troubled at night with asthma-like attacks of dyspnœa. By the end of September he began to be drowsy. His temperature varied, but never exceeded 101°. His bowels were opened regularly, and were rather loose. The urine was usually scanty, about 20 oz. in twenty-four hours. The drowsiness increased, and he died comatose on October 6th.

AUTOPSY, October 7th.—*Heart* 14 oz.; right side full of clots; left ventricle empty, contracted; valves thickened, but competent; left ventricle hypertrophied; heart's muscle generally pale, soft, and friable.

Lungs.—Turbid yellow serum in pleural cavities; right, 300 ccs., left, 100 ccs. Right lung adherent to diaphragm. Both lungs emphysematous in front, œdematous, congested, and in parts collapsed posteriorly. *Scattered through the left lung* were patches as large as a bean, some fresh and vascular, others pale greyish and gelatinous-looking, trabeculated and puriform in the centre, which under the microscope showed pulmonary alveoli filled with fibrin, round cells and desquamated epithelium. In both lungs there was generalised bronchitis, with dilatation of the larger bronchi and peribronchial thickening.

Liver 42 oz.; capsule thickened and adherent to diaphragm. On section, congested, soft and friable.

Spleen 3½ oz.; capsule thickened.

Kidneys 8½ oz.; both kidneys atrophied; capsules adherent; surfaces granular. On section, cortex diminished, of a brown red colour, dotted with grey and yellow points; medullary portions of a darker hue.

THE ALIMENTARY SYSTEM.—*Catarrh of the stomach* is a very common complication. It is generally not very intense, giving rise to flatulence, weight after food, and attended by morning sickness or nausea. There is often some chronic pharyngeal catarrh associated with it. The bowels are generally *confined*, and the action of the liver sluggish. Sometimes constipation alternates with attacks of *diarrhœa* due to intestinal catarrh. Biernocki has found that there is generally diminished gastric secretion, free hydrochloric acid is scanty or absent, pepsine too may be absent, but the motor activity of the stomach is increased. *Hæmatemesis* and *hæmorrhage*

from the bowel occur occasionally. *Hæmorrhoids* are not uncommon. The *liver* is generally diseased, most commonly fatty, often more or less cirrhosed or congested, or shows signs of lardaceous degeneration; in some cases the liver has undergone simple atrophy. Hanot has described a hypertrophic condition which he calls the uræmic liver and attributes to the nephritic dyscrasia.

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CHAPTER XIV.

THE TREATMENT OF BRIGHT'S DISEASE.

SUCCESSFUL treatment depends in the first place upon a correct knowledge of the principles of diagnosis and prognosis which have been laid down. We are all liable to try to do too much in the way of treatment. This arises from our ignorance of the exact nature and probable course of diseases, and our consequent uncertainty as to their result. Our pathological conception of Bright's disease having undergone some modification during the last twenty years, it follows that our treatment, so far as that was based on theoretical considerations should be changed also. If we would understand rightly the path by which we have reached our present stand-point, we must remember that at and for many years after Bright's time, albuminuria was held to be synonymous with a grave alteration in the kidneys. It is only within the last twenty years that it has been reduced to its proper position as one of the symptoms of Bright's disease, but which may occur when no such changes exist in the kidney, and that its amount is neither directly nor indirectly a measure of those changes or of the condition of the patient. Moreover, we no longer dread the drain of albumen from the system ; we know that the loss rarely exceeds half an ounce of dry albumen *per diem* and that there are on record many cases in which albuminuria has lasted twenty years or more without appreciably impairing the patient's health. We have realised that kidneys which have been damaged by inflammation, permit the passage of albumen for a long time after the inflammatory process has ceased to be active, and we no longer look upon albuminuria as an inflammatory exudate, but as evidence of an alteration, transient, persistent, or even permanent in the walls of the renal vessels. We recognise that acute Bright's disease in previously healthy persons, is a highly curable disease and that there are forms of chronic Bright's disease, such as those occurring after repeated pregnancies, in which a cure may be hoped for if a recurrence of the cause can be avoided. We reserve our grave prognosis for two classes of

cases, (1,) those in which the amount of disease present is excessive, and (2,) those in which we are unable to remove the persistent and efficient cause. We judge of the amount of renal disease, not by the quantity of albumen in the urine, or even by the tube casts, but by the evidence of cardio-vascular and retinal change, and by the general constitutional state. The most persistent cause is the lithæmic or gouty dyscrasia, which we are, unhappily, too often unable to remove. These cases are grave, and are liable to numerous serious and often fatal accidents, yet they often last a long time under judicious management.

What are the conditions under which the patient should be sent to bed?—Whenever there is dropsy or the urine diminishes, or the albumen is greatly increased, or any inflammatory complication comes on, or there is marked dyspnœa, or any sign of uræmia, it is prudent to send the patient to bed, as it is better to err by being a little over-careful.

The treatment of symptoms should not be undertaken too vigorously. Minor ones that are not causing distress are often best let alone, unless they are regarded as danger signals, when a few days' rest in bed on simple diet and treatment will afford oportunity for judging of their value and of what is needed to be done. We should recognise the incurable nature of certain symptoms and avoid treating them. Of two remedies or methods of treatment we should choose that which is the less debilitating.

If a patient suffering from chronic Bright's disease is in fair general health, and the discovery of the lesion has been made more or less by accident, we should be careful to do nothing that will worsen his condition either by over vigorous treatment or too severe regimen, but should be content to relieve the symptoms of which he complains, if it is in our power to do so, while at the same time we endeavour to regulate his habits and mode of life in conformity with principles deduced from our knowledge of the etiology and pathology of his disease, and confirmed by clinical experience.

CLIMATE AND HYGIENE.—It is seldom that our patients have it in their power to choose their residence in strict conformity with medical advice, but where it is possible they should seek a dry warm climate for the winter. Algiers is uncertain, as the weather is liable to sudden changes from an English summer climate to deluges of rain with cold wind. Egypt is often bitterly cold, but is dry. The uplands of

South Africa are a long way off, but as our winter is their summer they afford the invalid who is in fair health and can make the change, the opportunity of enjoying two summers, while residence there all the year round fulfils the required climatic conditions. If the patient stay at home, his house should be on a dry soil, and sheltered from the north and north-east winds. Our south coast health resorts, St. Leonards, Ventnor, Bournemouth and Torquay, do not fulfil all the requirements of climate, but offer during the winter, shelter, a comparatively mild climate and a moderate rainfall.

During the summer months Europe is less difficult, and a visit to the Black Forest, the Engadine, or to Braemar or Buxton, is greatly calculated to improve the general health, and should be undertaken especially by those unable to get away in the winter.

Clothing.—The patient should wear woollen clothing by day and by night, summer and winter, and in all climates. The adoption of the so-called "Jaeger system" is perhaps the very best thing these patients can do.

BATHS AND BATHING.—The use of the *hot air* or *vapour bath* in their own rooms once a week is better than taking a Turkish bath away from home. After the bath the patient should be well rubbed down and then go to bed. The duration of the bath should not exceed twenty minutes. The skin may not act well the first few times, but will gradually acquire activity. If the duration of the bath is prolonged it may cause faintness.

Cold bathing or *sponging* should be avoided, but tepid sponging every morning may be allowed.

EXERCISE.—Daily *exercise* should be encouraged, but violent exercise, such as running or anything approaching fatigue, is to be avoided, having in view the state of the heart and vascular system.

DIET.—The proper diet for acute Bright's disease is *milk*, with the addition of a certain amount of farinaceous matter to supply the alkalies so necessary to the body; the quantity of milk should not exceed three pints daily. This is the diet which we should always be prepared to fall back upon, in all serious complications, but valuable as it is in its proper place it is not a good or useful regimen when the patient can with satisfaction and safety take a more varied, and therefore more agreeable, less bulky, and more sustaining diet.

As the acute stage passes off, vegetables and fruits, eggs and

light meats, should be gradually introduced, and when the disease is chronic the only general restriction to be laid down is: *eat sparingly of butcher's meat, and avoid spirits, malt liquors, and strong wines.*

The safest drinks are the light Moselle, Rhine, or Bordeaux wines neutralised by the addition of an alkaline mineral water.

Ordinary drinking water generally contains a considerable quantity of sulphate of lime, at any rate in this district, and I am convinced is very hurtful. The mineral waters may be the distilled table waters, or Contrèxeville, or Vichy water. If the ordinary water supply is very hard, distilled water or filtered rain-water should be used for making tea, coffee, etc.

Beef tea and soups of all kinds should be interdicted; the former has a chemical composition closely resembling that of urine (MASTERMAN), and all soups partake more or less of this character, unless they are made without any stock, as some German soups are made, but these are hardly understood by the British cook.

By every means endeavour to keep up the patient's general health and nutrition, and set aside any of the above injunctions which interfere with these all-important considerations.

DRUGS.—In the absence of any specific remedy I generally order:—

℞ Ferri Sulph. gr. iij
Magn. Sulph. gr. xl
Ac. Sulph. dil. ♏iij
Aq. Menthæ pip. ℥j

Sig. To be taken three times a day.

or

℞ Tr. Digitalis ♏x
Pot. Iodidi gr. v
Sp. Ammon. Aromat. ♏xv
Aq. ad ℥j

Sig. To be taken three times a day, with the occasional use at bed time of the following pill:—

℞ Euonymin gr. j
Ext. Aloes gr. ij
Ext. Belladonnæ gr. ½

Albuminuria.—In the last edition of his *Urinary and Renal Diseases*, Roberts repeats the question: "Are there any medicinal substances capable of exercising control over the quantity of albumen lost by the urine?" and he answers it as before, by saying: "Exact observations do not give an affirmative answer to this question."

Rosenstein deals with this question at length, and mentions a number of drugs tested by his assistant, Dr. Kooi and himself. He gives his opinion in the following terms : "The physician must be impressed with the idea that we possess no drug which can in any sense act upon the local disorder so as to diminish decidedly the excretion of albumen."

The action of drugs on diseased processes in the human organism is always an obscure and difficult problem, on account of the large number and inconstancy of the factors that enter into it. An exact observation demands identity of all conditions except the one to be tested, namely, the drug employed ; but that is impossible, for no two cases are identical, nor is the same patient this week in identically the same circumstances as he was a week ago, or will be a week hence; so we must always allow an element of uncertainty in our most carefully devised experiments with drugs in disease, and our conclusions must be based rather on wide experience than upon the minute observation of particular cases.

Nevertheless, I have endeavoured to combine these two methods ; I have made observations upon many cases, and have sought in the practice of my colleagues to learn the results of their treatment, so that by comparison I might eliminate the "personal equation" from my conclusions.

It is obviously essential to the proper treatment of this question that we should understand the natural course of the disease or symptom which we seek to influence with drugs. It is to my mind beyond question, and if necessary, I could quote cases to prove it, that in acute Bright's disease and even in subacute Bright's disease, the albumen may diminish and disappear without the use of any drugs whatever. Moreover, cases of chronic Bright's disease are liable to intercurrent acute exacerbations of greater or less intensity, which may clear up just like an acute attack in healthy organs, the subsidence being accompanied by a more or less rapid and considerable reduction in the amount of albumen excreted. Finally, cases of persistent albuminuria present fluctuations in amount which depend upon causes that escape our present powers of observation.

Besides distinguishing between these phases of disease and allowing as best we can for these fluctuations, we have to bear in mind that the amount of albumen is influenced by diet, increased by exercise, and diminished by the recumbent position.

Patients with Bright's disease are frequently also the subjects of other accidental or secondary organic diseases, such as heart, lung, or liver affections, which probably play some part in the production of albuminuria, and interfere with the action of the drugs we employ, or give rise to fluctuations which depend upon changes originating in altered states of those organs.

A more obvious source of fallacy, but one which is certainly apt to be overlooked in private practice is, that the amount of albumen excreted does not always hold the same relation to the quantity of water, so that diuresis, either spontaneous or the effect of drugs, often produces an apparent improvement in the albuminuria, though, in fact, it may remain the same, or be actually increased in amount. Another and less excusable error may arise from comparing samples of urine passed at different periods of the day, as it is well known that the albumen varies very much, being generally most in the forenoon, other conditions being equal. No comparison should be made for the purposes of exact observation, except between samples of the whole twenty-four hours' urine collected and mixed together.

I carefully endeavoured to meet all the difficulties I have enumerated, and to eliminate these sources of fallacy.

The quantity of albumen was estimated by Esbach's tubes, generally by myself, always under my supervision; and I would bear testimony to the constancy of the results obtained by this method, which also gives approximately correct quantitative results. Before Esbach's tubes were introduced I used test-tubes marked with a scratch, and measured by means of a scale, which afforded a rough means of estimating the amount of albumen.

Perhaps no cases afford a better opportunity for testing the influence of drugs than those of "functional albuminuria," where the albumen is persistent, and is unaccompanied by any other evidence of disease. Many of my patients, otherwise apparently healthy, have been applicants for Life Insurance, and both they and I have been anxious to remove what appeared to be the only obstacle to their acceptance. Yet I must admit that I have never been able to cure one of these insurance cases. After a few months of non-success, they have passed from under my observation, and I cannot now tell what has become of them. Even those cases of "functional albuminuria" which I have seen ultimately cured

by time, have not appeared to me to owe this result in any instance to the direct action of drugs.

Having made this general statement, I will submit my conclusions as to the actions of particular drugs a little more in detail.

Alkalies.—I have used alkalies in the form of diluents; for example, a quart of bitartrate of potash imperial (℥ss to Oj) daily, or a bottle of Vichy water (Célestins or Haute Rive); and in a series of chronic cases, with persistent and copious albuminuria, the results were distinctly favourable. In addition to these diluents, I have employed citrate of lithia, bicarbonate of potash, and benzoate and bicarbonate of soda, and I include them in this favourable opinion. This effect was not due to the formation of alkali albumen, as Esbach's fluid precipitates this. In the following five chronic cases, the average total amount of albumen passed on the first and last two days of the experiment are given.

Name.	*First Two Days.*	*Last Two Days.*
B.	38 grs.	21 grs.
R.	38 grs.	13 grs.
J.	123 grs.	64 grs.
McD.	52 grs.	48 grs.
St.	16 grs.	21 grs.

Tannate of Soda.—I found the drug supplied under this name so nauseous that I have used in its stead the following formula.

℞ Acidi tannici, sodæ bicarb., ℥ā gr. x; glycerini ♏xv; aq. ℥j. M. t. d. s. I can report in relatively favourable terms of it. For example:

Name.	*First Two Days.*	*Last Two Days.*
M.	198 grs.	150 grs.
J.	165 grs.	96 grs.

These were both chronic cases. In an acute case I got good results, but the influence of the drug was very doubtful here.

Name.	*First Two Days.*	*Last Two Days.*
Be.	22 grs.	11 grs.

Nitro-glycerine.—I have seen cases do remarkably well under the use of this drug; but I am not able to confirm this by exact observation, except in acute cases.

Name.	*First Two Days.*	*Last Two Days.*
Be.	26 grs.	10 grs.

In a chronic case I found:

Name.	*First Two Days.*	*Last Two Days.*
McD.	40 grs.	43 grs.

Fuchsin.—Under the most favourable circumstances I have been unable to observe results which bear out the reputation this drug has acquired.

Name.	*First Two Days.*	*Last Two Days.*
McD.	34 grs.	65 grs.
St.	66 grs.	74 grs.

I have used it in a very large number of cases, and I have never seen any good effected by it.

Digitalis appears to increase the amount of albumen, and this holds good of other heart-tonics, for example, *caffeine*, *strophanthus*, and *sulphate of sparteine*. *Iron*, including the acetate, sulphate, and perchloride, has the same effect of increasing the albumen. *Terpine*, in ten-grain doses, three times daily, in one case increased, in another did not diminish the albumen. *Apocynum* increased the albumen in two cases, and diminished it in one. I was not able to observe the remarkable diuretic effect of this drug (used as the tincture in drachm doses) which is claimed for it across the Atlantic. I have used *turpentine* in several cases, without being convinced of any beneficial result, though hæmaturia has followed the employment of even minute doses (one minim). The *bichloride of mercury*, recommended by Millard, of New York, and in use by the homœopaths, has had a fair trial in the suggested doses (gr. $\frac{1}{1000}$), but has entirely failed. *Purgatives* and *diaphoretics*, though of great value in its treatment, do not appear directly to influence the amount of albumen excreted in chronic Bright's disease.

The following is a list of drugs whose action on albuminuria was tested in these experiments. Bitartrate of potash, bicarbonate of potash, citrate of lithia, carbonate of lithia, bicarbonate of soda, benzoate of soda, tannate of soda, tannic acid, digitalis, scoparium, sulphate of sparteine, strophanthus, pilocarpine, Trousseau's diuretic wine, caffeine, apocynum, cannabinon, ergot, turpentine, terpine, copaiba, oil of sandalwood, fuchsin, anti-hydropin (pulvis blattæ orientalis), cantharides, iodide of potassium, chloral, spirits of nitrous ether, perchloride of iron, sulphate of iron, acetate of iron, acetate of lead, tartrate of antimony, sulphate of alum, bichloride of mercury, elaterium, jalap, scammony, guaiacum, and sulphur.

Hæmaturia.—Slight hæmorrhage from the kidneys is not of much importance; in acute congestion it probably does good, at any rate I believe I have noticed that acute cases in which some moderate hæmaturia has been very persistent have

eventually done very well, but when treatment is desirable a *sinapism* may be applied to the loins, or the same region may be *dry-cupped.*

Hæmostatic drugs are not very efficient. In urgent cases 2 or 3 grains of *ergotin* may be injected subcutaneously; or half-drachm doses of liquid *extract of ergot* given by the mouth, hourly if necessary, as in those cases of profuse hæmaturia which sometimes occur. Other remedies are *acetate of lead*, 1 to 3 grains every four hours; *tincture of hamamelis*, 15 to 20 minims every two to four hours; *gallic acid*, 10 grains every four hours.

Dropsy.—The knowledge we possess of the pathology of dropsy enables us at least to see what are the desirable points towards which to direct our treatment.

In the dropsy of acute nephritis and its consequences we should endeavour to keep the quantity of fluid swallowed within moderate limits, and to promote its evacuation by the bowels by the use of purgatives causing watery stools, of which one of the best is bitartrate of potash. This may be given as an electuary composed of one part of the salt to two parts of honey or syrup, a tea-spoonful for a dose, repeated until the desired effect is produced. Although an acid salt, it does not diminish the alkalinity of the blood serum, which would be very undesirable; and we may endeavour to maintain this by giving farinaceous food, with Vichy water and lemon juice as a drink.

Compound jalap, or compound scammony powder, or the resin of scammony may be used, but very drastic purgatives, such as elaterium, are not desirable.

Hot-air baths should be employed daily, or pilocarpine, gr. $\frac{1}{8}$, may be injected hypodermically, but in some individuals it causes intense salivation and little or no diaphoresis.

There need be no hurry to employ drainage, unless urgent symptoms arise; if there be much fluid in the serous sacs this can be drawn off by a fine needle with tubing attached, but the cellular tissue is less easy to drain; cellulitis is sometimes set up by the attempt, and I have seen the effusion apparently poured out as fast as it was drawn off by the small trochars of Southey, so that although there was a considerable amount of fluid withdrawn the œdema did not lessen. If it has to be done, these small trochars with tubing attached are to be preferred to incisions, however small. In obstinate dropsy of the lower extremities I have observed the very best effects follow elevating the limbs, rubbing them towards the body so as to get

as much fluid as possible out of them, and then enveloping them in flannel bandages from the toes to the upper part of the thighs.

Œdema of the *prepuce* and *scrotum* may be relieved by several *punctures* with a darning needle; the parts afterwards being wrapped in absorbent cotton wool.

Œdema of the glottis is treated by *ice* to suck, *puncture*, and, in the last resort, *tracheotomy*. It is possible that *intubation* of the larynx might be effectual in relieving this symptom.

The action of the kidneys should be promoted by hot poultices to the loins, by diuretics, such as acetate of potash, squill, caffeine, digitalis, triticum repens, broom-tops, Trousseau's diuretic wine, etc., but diuretics are very uncertain remedies.

In the dropsy of chronic lithæmic nephritis we have to deal with a *failing heart*, and our chief reliance must be upon drugs that increase its energy. Digitalis takes the first rank; if there is aortic regurgitation convallaria, in 15 minim doses of the tincture, is a good drug; either may be combined with 5 grains of citrate of caffeine, 10 grains of sodium salicylate, 1 minim of nitro-glycerine solution (1 per cent.), and an ounce of infusion of broom-tops.

If there is peritoneal effusion this may be removed by tapping. Pleural effusions should not be rashly interfered with, especially if there is reason to believe they are not recent.

These cases are eminently unsuited for purging; it is sufficient to keep the bowels open; for it must be remembered that when dropsy sets in from heart failure, the end is very near, and may be more easily precipitated than averted.

Uræmia.—Headache and *giddiness* are relieved best by citrate of *caffeine*, 1 to 5 grains, or *nitro-glycerine*, 1 to 2 minims of the 1 per cent. solution in a little water. To ward off uræmic attacks, *sodium benzoate* may be given. Thomson reports favourably of *benzoic acid*.

All the minor phenomena of uræmia—*blindness*, *deafness*, *cramps*, *formication*, *numbness* and *palpitation*, should be treated by a smart *purgative* and the *hot air bath*, or the injection of $\frac{1}{12}$th of a grain of *pilocarpine* under the skin. *Palpitation* may be relieved by nitro-glycerine.

Convulsions, if soon over, scarcely call for treatment; they may be stopped by *chloroform* inhalation, or by *chloral* (gr. xx) injected into the rectum, and small doses (gr. v to x) of the same drug may be given every three or four hours to prevent their return; the skin should be got to act by the *hot air bath* or *pilocarpine*, and the *bowels* freely moved.

In obstinate convulsions, 12 to 16 ounces of blood may be taken from the arm.

Hemiplegia and *coma* call for bleeding to the like amount, but the *hot air bath* recovered one patient from coma after the attempt to bleed had failed.

It has been suggested to treat uræmia by dilution of the blood, as has been practised in diabetic coma, and a case has been quoted in which temporary improvement followed the adoption of this plan.

Vomiting and *diarrhœa* are natural efforts at elimination which should not be too quickly checked.

Uræmic asthma is not at all amenable to treatment. Carter, of Liverpool, recommends drachm doses of *ozonic ether* in liq. ammoniæ acetatis, but it has not proved of any service in my hands. Inhalations of *oxygen* have been recommended, but are not very successful. The ordinary treatment for uræmia may be tried. *Nitro-glycerine* or *nitrite of amyl* affords some relief. *Ethyl-nitrite* may be tried in half-drachm doses of a 3 per cent. solution (LEECH). Roosevelt has recommended *cobalto nitrite* of potassium in half-grain doses every two to four hours. Stephen Mackenzie has advocated the plan originally suggested by Loomis of injecting morphine hypodermically, and W. Carter has added the indication to choose for this treatment those cases in which the pupils are dilated.

Epistaxis and other external hæmorrhages are best treated by *ergotin*, two to three grains, injected under the skin, or *ergot* may be given by the mouth. An *ice-bag* may be applied locally.

Inflammatory Complications.—Pneumonia, pleurisy, pericarditis and *peritonitis*, are of most unfavourable prognosis. Very active treatment is hardly judicious. *Poultices* or *hot fomentations* should be applied locally, and the case managed on general conservative principles.

Gastric Catarrh.—This symptom is often very troublesome. Fats, raw vegetables and uncooked fruits should be eliminated from the diet; a tea-spoonful of *Pulv. Sodii Sulph. Effervesc.* (*B.P.*) dissolved in half a tumbler of warm water should be sipped each morning before breakfast, and the following powder given in a little milk shortly before each meal:—

℞	Bismuthi Carb.	gr. x
	Sodii Bicarb.	gr. x
	Pulv. Rhei	gr. ij
	Pulv. Cinnamoni Co.	gr. v

Fiat pulvis.

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SECTION II.—THE URINE.

CHAPTER XV.

CLINICAL EXAMINATION OF THE URINE.

INSPECTION of the urine is an ancient practice, which, for the most part, was until recent times a meaningless and perfunctory medical ceremony.

Healthy urine is a clear, bright yellow fluid, having a not disagreeable but characteristic odour. It is liable to many alterations of quantity, physical properties, and chemical composition; so that in judging of a given specimen it is necessary to pursue a methodical enquiry.

The following table copied from Salkowski and Leube gives a summary of the substances met with in normal urine:—

I. ORGANIC.—(1,) Substances belonging to the fatty series: —Urea; uric acid; xanthein bodies; kreatin and kreatinin; oxalic acid; oxaluric acid; volatile fatty acids; glycerinphosphoric acid; sulphocyanic acid; lactic acid.

(2,) Substances belonging to the aromatic series:—Hippuric acid and benzoic acid; sulpho-carbolic acid; cresolsulphuric acid; sulpho-pyrocatechuic acid; paraoxyphenylacetic acid; parahydrocumaric acid; sulphindigotic acid; skatoxyl-sulphuric acid; cyanuric acid.

(3,) Substances which apparently belong to neither:—Urobilin; sulphur compounds; pepsin; left rotatory substances; cryptophanic acid; extractives.

II. INORGANIC.—Sulphuric acid; hydrochloric acid; phosphoric acid; sodium; potassium; ammonium; magnesium; calcium; iron; nitric acid; nitrous acid; peroxide of hydrogen; gases.

PHYSICAL PROPERTIES. *Quantity.*—The quantity of urine in health is usually from 40 to 50 ounces, but it may be occasionally as low as 25 or as high as 70 or 80 without indicating disease. In females it is probably less than in males.

Yvon and Berlioz give as the mean of their observations 45 oz. (1360 ccs.) in males, and 36 oz. (1109 ccs.) in females, a proportion of five to four. Under pathological conditions the daily quantity may rise to 40 or 50 pints (*polyuria*); on the other hand it may be reduced to a few ounces (*oliguria*), or completely suppressed (*anuria*). In all diseases of the heart or kidneys it is of especial importance to have the urine measured daily; and in hospital practice it should be the rule to have the urine of all patients measured on admission, and from time to time during their stay. Urine-measures of white carthenware can now be procured which have a vertical scale on the inside. The whole of the urine for twenty-four hours is collected in one of these, and the amount read off from the scale. In this country we usually measure by fluid ounces; on the continent they measure more accurately by cubic centimetres, of which about thirty make a fluid ounce.

Our method is not very exact, but it is not necessary to be so when the urine is fairly abundant; if it is scanty it can be measured more accurately in a glass graduated to cubic centimetres.

The daily amount of urine should find a place on the temperature chart, with the pulse, respirations, and movements of the bowels.

Odour.—The odour of normal urine is peculiar; it has been described as "fragrant" and "aromatic"; and no attempt will be made here to add to these definitions. Certain articles of diet, *e.g.*, garlic and asparagus, communicate to it a very disagreeable smell of sulphides. Turpentine gives it the odour of violets, not only when taken internally, but when the vapour is inhaled, as in polishing furniture or as a medication for bronchitis. Copaiba and cubebs cause the urine to have a peculiar and quite characteristic odour.

Fermentative decomposition inside or outside the body is usually alkaline; by the decomposition of urea, ammonia is set free which has its own well-known smell. In diabetes the urine sometimes has a sweetish smell like hay. Urine containing decomposing blood or pus may have a positively putrid odour like decayed fish or flesh.

Translucency.—Normal urine is clear and bright when freshly passed, but may become turbid from precipitation of *urates*, which are insoluble in excess, in the cold. On standing, it may become turbid from decomposition, permitting phosphatic precipitation, or the growth of micro-organisms.

Urine may be turbid when passed from the presence of phosphates; such urine is alkaline, and if it is persistent the condition calls for treatment.

Other causes of turbidity are the admixture of mucus, pus, or blood, decomposition in the bladder, and the presence of fat (*chyluria*).

Colour.—The colour of normal urine may vary from the reddish yellow urine of digestion (*urina cibi*), to the nearly colourless urine which follows free potations (*urina potus*).

The normal urinary pigments have not been completely determined, only two being known, α—urobilin, and β—indican.

Urobilin is formed indirectly from blood-colouring matter (hæmatin). The hepatic cells convert the hæmoglobin first into hæmatin and then into bilirubin; bilirubin is oxidised into urobilin and excreted by the kidney.

Febrile urobilin is an imperfectly oxidised form met with in fevers and in cirrhosis of the liver.

Variations in the yellow colour of urine are for the most part dependent on the proportion of urobilin present.

Indican is the substance formerly called uroxanthin; it gives the urine a deep yellow colour, but if it becomes oxidised in decomposing urine a film of bluish red crystals of indigo-blue is formed. It is a product of pancreatic digestion.

Certain drugs taken internally give rise to alterations of colour; *e.g.*, *rhubarb*, deep yellow; *santonin*, golden yellow; *chrysophanic acid*, orange yellow; *senna*, brownish; *logwood* and *fuchsin*, reddish; *methylene-blue*, blue; *carbolic acid*, *tar*, and *creasote*, brown or black. Carbolic acid dressings produce the same effect, if the carbolic acid is in excess.

Vogel describes black discolouration of the urine after poisoning by *arseniuretted hydrogen.*

The urine may be coloured *red* by the admixture of *blood*, the tint being deep in proportion to the quantity present; or *brownish*, ranging from smoky to porter coloured, from the formation of methæmoglobin, if the urine has had time to act upon the blood.

In jaundice, *biliary colouring matter* (bilirubin) is excreted by the kidneys, giving rise to various tints of *saffron yellow*, *mahogany brown*, or *dark olive green.* When jaundiced urine has been kept some days it may change to a *grass green* colour (biliverdin), from oxidation of the biliary pigment (ROBERTS).

Pus and *fat* (chyluria) give the urine a cream colour, while

affecting its translucency. In diabetes the urine is of a *pale greenish* colour. In melanæmia the urine is often *dark brown*. A *blue* colour on the surface is due to crystals of indican.

Darkening of the urine may also be due to alkapton, pyrocatechin, protocatechuic acid, uroleucic, and uroxanthic acids.

Density.—The *density* or *specific gravity* of normal urine is usually from 1·015 to 1·025, but the clear limpid *urina potus* may be as low as 1·005 or less in healthy persons, while urine concentrated owing to free action of the skin in warm weather may be 1·028 or even 1·030.

The normal amount of solids in the urine is about 4 per cent., of which the chief components are urea and common salt; but the proportion of solids to water varies greatly in health, and still more in disease. In a case of post-scarlatinal nephritis W. G. Smith has recorded a urinary density of 1·065; in diabetes mellitus it is generally over 1·030, often over 1·040; in chronic Bright's disease it is usually under 1·015, while in contracting kidney and diabetes insipidus it is very little over 1·000.

The *density* is estimated by means of a *urinometer*, an instrument too familiar to need special description. It is floated in the urine, and the density is read off upon a vertical scale. These instruments are not very accurately made; it should repay some instrument maker to give special attention to their construction.

The urine to be examined should be a sample of the whole *mixed urine* for twenty-four hours, a point very commonly neglected and not always attainable; but it may be remembered that great variations occur in the urine in different periods of the twenty-four hours, so that too much importance must not be made of the result obtained from a stray sample, as in Life Insurance examinations.

If there is too little urine to float the urinometer, the examination may be postponed till it is completed on other points, and then one or more equal quantities of distilled water added till the instrument floats; the last two figures of the result must be multiplied by the number of dilutions to give the true density.

The following precautions in the use of the urinometer should be noted:—

(1,) The glass must not be too narrow. There should be at least half an inch between the stem of the instrument and

the side. The cylindrical glasses supplied with urinometers are frequently too narrow.

(2,) The instrument must float freely.

(3,) The surface of the urine should be free from froth; bubbles may be removed by blotting paper.

(4,) The instrument should be free from grease.

Reaction.—Healthy urine is generally *acid.* This is due to the presence of acid phosphate of soda. When this salt is submitted to dialysis, a larger amount of phosphoric acid is found on the outside than on the inside of the dialyser, showing that the acid diffuses faster than the base; this experiment may serve to explain how it is we get an acid secretion like urine from alkaline blood. When the urine is *alkaline* this salt is replaced by alkaline phosphate or by ammonia.

The degree of acidity varies, being diminished partly by food, even so as to render it actually alkaline.

This maximum effect is reached two or three hours after a meal; but, as Roberts points out, no alkaline urine may be voided, because it is mixed in the bladder with acid urine secreted before the meal, or remains there until acid urine is again secreted in a quantity sufficient to modify the reaction.

This alkalinity is due to the presence of fixed alkalies and alkaline earths; on the other hand, the urine passed early in the morning, when many hours have elapsed since the last meal, is excessively acid, but prolonged fasting does not intensify this.

Vegetable and mineral acids increase the acidity of the urine. In phosphaturia, where amorphous earthy phosphates are passed in alkaline urine, this condition can be speedily remedied by the use of nitro-hydrochloric acid; but where the alkalinity is due to fermentative decomposition in the bladder, acids administered internally fail to correct it, probably because they can be given in such small quantities only. The urine is highly acid in gout and allied digestive disorders, in diabetes, acute rheumatism, and chronic Bright's disease.

Alkaline substances readily make the urine alkaline, but the quantities must be large. Roberts says it requires three to four hundred grains of bicarbonate, acetate or citrate of potash, given in divided doses during twenty-four hours, to keep the urine of an adult steadily alkaline.

Lithia is the most powerful base for producing alkalinity of the urine.

Prolonged immersion of the body in a cold bath is said to render the urine alkaline. The urine is frequently alkaline in debility and debilitating diseases, and in the peculiar form of atonic dyspepsia of nervous origin, in which earthy amorphous phosphates are excreted in large quantities.

In all the above cases the urine is alkaline from salts of potash, soda, and the alkaline earths.

Ammoniacal urine is due to decomposition of urea under the influence of a special ferment; this takes place either in the bladder or in the vessel in which the urine is kept after it is voided. Where there is no suspicion of bladder disease the latter possibility should always be excluded by procuring a freshly passed specimen of the urine.

The reaction of urine is estimated by *litmus* paper. This is generally sold in two colours, red and blue, but the latter is alone required, as it soon turns more or less red-violet, and is then most delicate. *Acids* turn litmus paper *red*, while *alkalies* turn it *blue*; the red-violet paper indicates both these changes better than quite blue or quite red paper can do.

Yellow turmeric paper is turned *brown* by alkalies, but it has no special advantage.

Quantitative estimation of the acidity can be performed by means of a standard solution of caustic soda (1 to 10 of water) which is placed in a burette and allowed to run into a beaker containing 100 ccm. of urine, the reaction being tested from time to time by litmus paper till the urine is neutralised. Multiply the number of milligrammes of fluid employed by 0·0063, the quantity of oxalic acid required to neutralise 1 ccm. of the standard solution, and the result gives the percentage acidity (calculated as oxalic acid). For comparative purposes this is quite sufficient.

CHEMICAL COMPOSITION. *Chlorides.*—Common salt or sodium chloride (Na Cl) forms about one fourth of the total solids of healthy urine, and gives the salt taste to this secretion. It is derived from the blood serum, in which it constitutes about 4 parts per 1000, and ultimately of course from the food. It is increased in *ague*, in *diabetes insipidus* and in *Bright's disease*. In Bright's disease complicating pneumonia this increase is not observed (NAUWERCK). It is diminished in *pneumonia*, and in all *febrile* diseases, especially if accompanied by an *exudation*; also in *chorea* and *pemphigus*. In pneumonia a vicarious increase of chlorides is said to be found in the sputa (THUDICHUM).

Chlorides are roughly estimated by precipitating the urine with a 10 per cent. solution of *nitrate of silver*, the resulting chloride of silver occupying in healthy urine nearly the whole column of fluid. In pneumonia there is scarcely any precipitate at all.

The quantity of chlorides is not of much importance as a clinical sign, and this method is sufficient for ordinary purposes. If more accurate estimation is required the operation must be performed with a standard solution of silver. The urine having been previously acidulated with nitric acid is repeatedly precipitated and filtered till no further precipitate forms. In accurate experiments the *ash* from a given quantity of urine should be employed.

The quantity of chlorides excreted daily is about ten to twelve grammes.

Phosphates.—From thirty to ninety grains of *phosphoric acid* are daily eliminated by the kidneys.

Acid phosphate of soda ($NaH_2PO_4 + H_2O$) gives, as already stated, the acid reaction to urine; a potash salt is also present in small quantity; they are both soluble salts. Phosphoric acid is also combined with *lime* and *magnesia*, forming salts which are soluble in acid urine, but precipitate out when it undergoes alkaline fermentation.

When urine is boiled a milky cloud often forms which is dissolved on cooling, or on the addition of a drop or two of acid. This cloud is due to phosphates, and the change that takes place is explained thus by Walter G. Smith :—

$$2\,(\underset{\text{soluble.}}{Ca_2H_2P_2O_8}) + \underset{\text{soluble.}}{CaH_4P_2O_8} = \underset{\text{insoluble.}}{Ca_3P_2O_8} + 2\,(\underset{\text{soluble.}}{CaH_4P_2O_8}).$$

On cooling, this process would be inverted.

Salkowski has pointed out that this chemical change may be imitated by a carefully prepared solution of acid calcium phosphate treated with ammonia till a precipitate forms, to which a few drops of acid phosphate are added and the liquid filtered; this solution gives a cloud on boiling, which redissolves on cooling or acidulation.

This phosphatic cloud is generally met with in the urine of patients whose digestive powers are feeble or overtaxed, but it is not of serious importance.

A peculiar greenish phosphatic deposit is described by Ehrlich in the urine of typhus, typhoid and measles, when treated with an acid solution of sulphanilinic acid, alkalinised

with ammonia, and allowed to stand for twenty-four hours. He regards it as characteristic of these diseases.

When a solution of ferric chlorides is added to urine a brownish precipitate frequently forms, soluble in excess, due to *phosphate of iron.* This reaction is employed for estimating the phosphoric acid in urine.

An increase of the total phosphates has been observed in acute inflammatory diseases of nerve structures, and temporarily in acute febrile diseases (VOGEL, TEISSIER), occasionally in acute mania and brain tumours, also in chorea, acute yellow atrophy of the liver (BOUCHARD), diabetes (LECORCHÉ), phthisis, chronic rheumatism, leucocythæmia and osteomalacia, and as a primary condition in certain cases of so-called phosphatic diabetes (RALFE, TEISSIER).

A diminution occurs in chronic brain disease, chronic disease of the heart or kidneys, in chlorosis, ague (GEE), rickets, and gout.

The excretion of phosphoric acid is increased by lactic acid and carbonate of soda, diminished by morphia, chloral, ether, chloroform, bromide of potassium (SCHULTZE), and alcohol.

Phosphates of the alkalies do not form urinary deposits, but earthy phosphates are met with as deposits in three forms: (1,) Ammonium magnesium phosphate, or triple phosphate; (2,) Crystalline phosphate of lime; (3,) amorphous phosphate of lime.

Ammonium-magnesium phosphate or *triple phosphate* ($MgNH_4PO_4 + 6H_2O$) crystallises out in triangular prisms with bevelled ends (*Fig.* 29) in urine which has undergone ammoniacal decomposition, forming a *white* deposit at the bottom of the glass. It may be met with in examining the mucous deposit of a urine which gives an acid reaction, decomposition commencing around the mucus. As a rule this deposit signifies only that the urine has decomposed in the vessel after leaving the body, but it may be met with in fresh urine which has undergone fermentation in the bladder, in cystitis, calculus, myelitis, etc. It is the special constituent of secondary calculous formations, on a nucleus of uric or oxalic acid; or as an incrustation on the walls of a diseased bladder, etc.

Fig. 79.—Crystals of triple phosphate. One prism is incomplete.

Crystalline phosphate of lime. Acid phosphate of lime ($CaH PO_4$) occurs in feebly acid urine. It is met with in

phthisis, cancer of the stomach and rheumatism, but it may be present in the urine of healthy persons. Its crystals take the form of rods, stars, rosettes, crosses and feathers (*Fig.* 30), hence the names of *stellar* or feathery *phosphate*. It is a somewhat rare deposit.

Fig. 30.—Crystalline phosphate of lime, showing cross, rosette, rod, and feather.

Neutral phosphate of lime ($Ca_3(PO_4)_2$) occurs in neutral or alkaline urine as an iridescent film on the surface. It has no clinical significance.

Amorphous phosphate of lime ($3CaO\ PO_5$) commonly occurs in urine which is alkaline when passed. It makes the urine turbid and deposits as a copious white sediment, readily soluble in acids. Under the microscope it consists of irregular granules and lumps (*Fig.* 31); on standing, crystals of triple phosphate soon form in it.

Fig. 31.—Amorphous phosphate of lime.

It is met with in healthy urine rendered alkaline by food, and in persons who are taking alkalies. As a persistent occurrence it is specially associated with a form of atonic dyspepsia, first described by Prout, which is greatly benefited by a course of hydrochloric acid or nitro-hydrochloric acid taken regularly after meals.

Carbonate of lime ($CaCO_3$) occurs as an amorphous deposit with earthy phosphates; its crystalline form is very rare. They are spherical bodies composed of numerous radiating needles (*Fig.* 32).

Fig. 32.—Crystalline carbonate of lime (after ROBERTS), spherules and dumbells formed of radiating rodlets.

Sulphuric acid occurs in very small quantities in the urine combined with alkalies, as *sulphates*, and with indol, skatol and pyrocatechin as aromatic ether-sulphuric compounds.

Sulphuric acid is chiefly derived from the decomposition of proteids, hence its amount runs parallel with the amount of urea excreted (LANDOIS).

The test for it is a solution of *barium chloride*, which gives a copious precipitate of barium sulphate, insoluble in nitric acid; Freund has suggested the addition of alizarin-sulphonate of soda to the urine which is then tritrated with baryta water, and the sulphates thrown down as a purple red precipitate; by this means the amount can be estimated.

Sulphur occurs also in cystin, in the sulpho-cyanogen compounds, etc.

Urea (CH_4N_2O). This substance is present in the urine in a larger quantity than any other solid. Its formation is a function of the liver, and its principal source is the nitrogenous matter taken as food, but it is also formed from the destruction of red blood corpuscles (in the liver) and other tissues, muscle albumen, etc.

The formation of urea is increased by a close atmosphere, such as a kitchen (COOK), by pepsin, maltin, common salt, phosphorus poisoning, arsenic, sulphuric acid, chlorate of potash, hot baths, by excess of nitrogenous food, by coffee, by drugs which stimulate the functions of the liver, *e.g.*, euonymin, corrosive sublimate, salicylic acid, benzoic acid, colchicum, by fever, by active congestion of the liver without destruction of its substance, by pernicious anæmia, malaria, etc. It is not increased by muscular exercise.

Its elimination is proportional *(cæteris paribus)* to the amount of urine excreted, so that copious drinking of water or any fluid, increases the elimination of urea ; it is also increased in diabetes mellitus and insipidus. Willis described and Prout believed in a pathological condition characterized by excess of urea excretion to which the name *azoturia* was given, but there is no such disease as an independent condition.

The formation of urea is diminished by fasting, by drugs which depress the function of the liver, *e.g.*, lead, and by those diseases of the liver which depress its function or destroy its substance.

Its elimination is checked by anything which diminishes the amount of urine, by profuse sweating, by diseases of the kidneys and urinary apparatus, by wasting diseases, acute gout, chronic rheumatism, lepra, pemphigus, melancholia, imbecility, catalepsy, hysteria, and cholera. It is supposed by some that the excretion of urea is diminished in a very early stage of contracting Bright's disease, before structural alterations have occurred in the kidney ; but this so-called *renal inadequacy* is quite fanciful.

The daily quantity of urea varies at different ages; according to Ralfe—

At	5	years	180 grains.
	12	„	320 „
	21	„	535 „
	40	„	555 „

Camerer gives the proportion in children at 0·64 to 1·12 grammes per kilogramme of body weight, while in adults the proportion is only 0·5 to 0·6 grammes per kilogramme.

Women excrete absolutely less than men, but not relatively in proportion to their weight.

The estimates for the inhabitants of different countries show variations, which are probably accounted for by differences in diet :—

Englishmen (RALFE) - - -	555 grains.
Bavarians (VOIT, RUBNER) -	425 „
Frenchmen (YVON, BERLIOZ) -	397 „
North Germans (FLUGGE) - -	352 „

One day's fasting is enough to reduce the urea excretion to two hundred and eighty-eight grains (RANKE), while after several days it falls to ninety grains (SCHULTZEN).

In acute Bright's disease, when the urine is greatly reduced, the elimination of urea is necessarily also diminished ; but the percentage of urea which should be high if there were merely a reduction of the urinary water, is *low*, generally below 2 per cent.

In sub-acute Bright's disease, as the urine increases in quantity the percentage of urea tends to fall lower, averaging about one per cent.

In the later stages the percentage of urea remains low while its total amount varies with the quantity of urine ; but as this is sometimes high it may reach a fair figure. On light diet, with chicken and fish, such patients may excrete from three hundred to four hundred grains of urea.

In the lithæmic form the urine throughout the early and middle course of the disease is much increased in amount, except during the occurrence of an intercurrent attack of acute nephritis, to which these cases are no doubt very liable. In these early stages and even later, the amount of urea may be normal.

W. S., aged twenty-three, was sent to me from the Eye Hospital with bilateral diffuse neuro-retinitis. He was admitted on the 24th February, 1888, and on the 26th his urine was analysed ; it amounted to seventy-eight oz. in twenty-four hours, and contained 0·8 per cent. of urea, equivalent to two hundred and ninety grains in twenty-four hours. On chicken diet he passed three hundred and seventy grains. He died in uræmic coma on April 7th, and his kidneys were found to be in a condition of advanced contraction. This case supports

the statements of Bartels, Grainger Stewart and others, that so long as there is polyuria, the elimination of urea may not be diminished.

Detection of urea.—The presence of urea may best be demonstrated by adding strong nitric acid to a little of the concentrated urine or other fluid in a watch glass, when crystals of nitrate of urea will form, which can be recognised by the microscope (*Fig.* 33); any albumen must be first removed by boiling and filtration.

Fig. 33.—Crystals of nitrate of urea artificially prepared by the addition of nitric acid to urine.

Estimation of urea.—The most convenient method of estimating urea is by decomposing it with *hypochlorite* or *hypobromite of sodium* solution, the amount of urea being determined by measuring the volume of nitrogen evolved. This method is sufficiently accurate for clinical purposes. The cheapest and simplest form of apparatus is that invented by Professor Doremus,

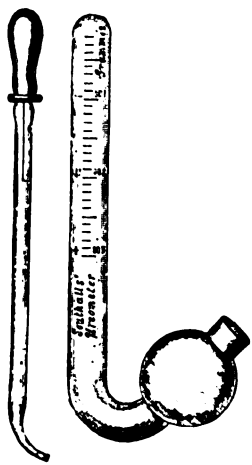

Fig. 34.

Fig. 35.

of New York, and sold by Messrs. Southall Brothers, Birmingham (*Fig.* 34).

The solution is poured into a tube till it half fills the bulb, then some urine is drawn up into the pipette as high as the

scratch, the beak of the pipette is carefully inserted into the curve of the tube, and the urine is made to flow by gentle pressure into the solution, the gas being given off and collected in the tube, where it is read off as a percentage. With a little care and practice there is very little loss, and the apparatus is most manageable and very inexpensive. An excellent ureometer is that known as Gerrard's, made by Messrs. Gibbs, Cuxson & Co., of Wednesbury (*Fig.* 35).

The solution is put into the bottle, and twenty ccm. of urine* are placed in the little tube. The apparatus is filled with water, and the surfaces of the fluid in the graduated tube and in the funnel at the side are brought to the same level by sliding the funnel up or down. Then by partially inverting the bottle the solution in the tube is brought into contact with the urine, the gas is liberated, and the result can be read off as a percentage on the scale.

The hypobromite solution is more energetic and rapid in its action than the hypochlorite. Its composition is one hundred parts of caustic soda, two hundred and fifty of water, and twenty-five of bromine. It will not keep well, and is better made fresh, but this is a very disagreeable process, and should be done out of doors, or in a stink-chamber.

The hypochlorite solution is simply the liq. sodæ chlorinatæ of the U.S. Pharmacopœia made by adding chloride of lime to a saturated solution of washing soda, and filtering or siphoning off the resulting solution.

In estimating the amount of urea it is essential to take a sample of the whole of the urine for twenty-four hours, as great variations occur in the amount of urea passed under different conditions. Thus the urine after drinking fluids freely is copious and contains a small percentage of urea, while that passed during digestion is concentrated and contains a great quantity both relatively and absolutely.

When great accuracy is desired the results should be corrected for temperature and pressure (NOEL PATON).

Uric acid ($C_5H_4N_4O_3$) is normally present in urine as urate of soda, which is not decomposable by the acid phosphate of soda to which the urine owes its acid reaction. If any free acid is liberated the urates are decomposed, and uric acid crystals are thrown down.

* Albuminous urine must be acidulated, boiled and filtered to remove the albumen before it is used for this test.

It is originally formed by the splitting up of albumen, but how and where this process takes place is doubtful, though a good deal of evidence points to the spleen as the seat of the change.

The normal daily amount excreted is seven to ten grains; it is not increased by nitrogenous diet (GARROD). Cook found beef tea, Liebig's extract, pepsin, maltin, euonymin, and confinement in a close atmosphere increase the amount of uric acid.

It may be sometimes increased by excessive use of *milk*.

The urine of newly born children contains much uric acid; it is increased in febrile diseases, acute rheumatism, pneumonia, ague and malarial fevers, leucocythæmia, cirrhosis of the liver, and diabetes.

It accumulates in the blood in gout (GARROD), and is excreted in greater quantity after an attack.

Its excretion is increased by colchicum, corrosive sublimate and euonymin, diminished by salicylate of soda and benzoate of soda (NOEL PATON). It is also diminished in anæmia, chlorosis and gout, and by copious draughts of water, large doses of quinine, caffein, iodide of potassium, common salt, carbonate of soda and lithia, sulphate of soda, oxygen inhalation and slight muscular exertion (LANDOIS and STIRLING).

Crystals of *uric acid* form a deposit like cayenne pepper on the bottom or sides of the glass; if larger, they may look like crystals of brown sugar. They assume various forms,—lozenges, rhomboids, hexagons, stars, spikes, etc. (*Fig.* 36).

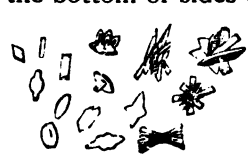

Fig. 36.—Crystals of uric acid in various forms.

The *murexide* reaction is the ordinary chemical test; a little of the suspected matter is heated slowly with a drop of nitric acid on a porcelain dish, and allowed to cool; a drop of dilute ammonia is then added, when a purple red colour due to *murexide* is developed if uric acid is present.

Quantitative estimation may be performed by adding five ccm. of concentrated *hydrochloric acid* to a hundred ccm. of urine and allowing it to stand for forty-eight hours in the dark, when the uric acid deposits and may be dried and weighed. Haycraft has devised a method by precipitating the uric acid as a silver salt, and Arthaud and Butte employ one which depends upon the formation of an insoluble urate with copper salts.

Amorphous urate of soda is normally present in urine, forming a reddish deposit in concentrated urine after it has cooled; it is also a common deposit in febrile diseases, and in cirrhosis and other affections of the liver. Under the microscope it appears as small irregular granules (*Fig.* 37), while on the addition of acetic acid uric acid crystallises out. According to Roberts it consists mainly of quadrurates which are readily decomposed by water, but this change is prevented by the salts of the urine, especially by the sodium chloride and potassium phosphate. Crystalline urates are rare.

Fig. 37.—Amorphous urate of soda.

Fig. 38.—Hedgehog crystals of urate of soda.

Crystalline urate of soda is sometimes deposited in the urine of children during febrile attacks. It forms characteristic yellow hedgehog crystals (*Fig.* 38). Roberts attributes the frequency of vesical calculi in children to this deposit.

Urate of ammonia is met with in ammoniacal urine; it has no clinical significance. It forms dark yellow spheres and pale slender dumbells (*Fig.* 39).

Fig. 39.—Urate of ammonia in dark yellow spheres, pale dumbells, crosses and rosettes.

Hippuric acid ($C_9H_9NO_3$) occurs to a small extent in human urine; it is formed when *benzoic* acid or some nearly related chemical body is introduced into the alimentary canal; and is also formed in the body from proteids (LANDOIS and STIRLING). It crystallises in colourless four-sided prisms (*Fig.* 40).

Fig. 40.—Crystals of hippuric acid from the urine of the horse.

In the herbivora it appears to replace uric acid to a great extent in their normal urine.

Kreatinin ($C_4H_7N_3O$) is derived from muscle kreatin; it is a normal constituent of urine. It may be detected by adding to the urine a few drops of a "slightly brownish" solution of nitro-prusside of sodium and weak caustic soda, when a Burgundy red colour is developed which soon fades. On heating with acetic acid the colour changes to green or blue.

It is increased in fevers, pneumonia, etc., diminished in anæmia and wasting diseases; it is not diminished by fasting.

Xanthin ($C_5H_4N_4O_2$) also occurs in normal urine in very small quantity. When evaporated with *nitric acid* it gives a

yellow stain which becomes yellowish red on adding *potash*, and red violet on heating.

It sometimes forms calculi, which are of a deep yellow colour, smooth and spherical.

Sarcin or *Hypoxanthin* ($C_5H_4N_4O$) has been found only in the urine of leucocythæmia, though a body nearly related to it occurs in normal urine (SALKOWSKI). When evaporated with *nitric acid* it gives a light *yellow* stain, which becomes deeper but not reddish on adding *caustic soda*.

Succinic acid ($C_4H_6O_4$) occurs chiefly after a diet of flesh and fat, after eating asparagus, and after drinking alcohol.

Lactic acid ($C_3H_6O_3$) is present in normal urine. Colasanti and Moscatelli found it present in large quantities in the urine of soldiers after a march, and they suggest that it is probably a product of muscular activity which passes into the urine.

Oxaluric acid ($C_3H_4N_2O_4$) is present in traces in normal urine combined with ammonia. It is a derivative of uric acid, and on being heated splits up into urea and oxalic acid.

Oxalic acid ($C_2H_2O_4$) is a normal constituent of urine, and in combination with soda and potash remains in solution. It is mainly derived from food, *e.g.*, tea, rhubarb, etc., but may be formed by the oxidation of uric acid into oxaluric acid ($C_8H_4N_2O_4$), which splits up into oxalic acid and urea.

Oxalate of lime ($C_2CaO_4+2H_2O$). Crystals of oxalate of lime can always be found among amorphous urates, if the urine has stood some time, but they may be deposited alone or with a little mucus in a very characteristic fleecy cloud; when not very abundant they may be seen glittering on what at first sight looks like a simple mucous cloud.

Oxalate of lime is formed by the decomposition of oxalate of soda and potash, and the union of the acid with lime salts.

A fleecy deposit of oxalate of lime crystals is associated with a special form of atonic dyspepsia to which the name of *oxaluria* has been given.

The precise conditions under which this deposit occurs cannot be formulated, but debility, anæmia, and various organic diseases of all kinds are predisposing causes. Over-eating under certain conditions may be a direct cause.

The crystals can readily be recognised under the microscope with a power of two hundred and fifty diameters by their

shape and high refractive powers. They are generally octohedral or pyramidal, more rarely dumbell shaped and not uncommonly spherical or oval (*Fig.* 41). These spheres are said by Roberts to be dumbells seen endwise, and Beale speaks of them as discs. I have frequently failed to see a single dumbell where these spheroids were visible, or to transform them into dumbells by shifting them about.

Fig. 41.—Crystals of oxalate of lime, octohedra, pyramids, dumbell and spheroid.

Cystin ($C_3NH_7SO_2$) is a left rotatory body which occurs normally in the urine in very small quantities, but very rarely in so large amount as to give rise to a deposit or the formation of calculi. The formation of cystin is associated with the presence in the urine and fæces of certain ptomaines belonging to the diamine class, *viz.* (*α*,) penta-methylene-diamine ($C_5H_{14}N$) (cadaverin), and (*β*,) tetra - methylene - diamine ($C_4H_{12}N$) (putrescin). These are due to the agency of certain specific intestinal bacteria, and some success has attended the treatment of cystinuria by the administration of salol and sulphate of magnesia to promote intestinal antisepsis. Cystin is recognised by its characteristic crystals in the form of hexagonal plates (*Fig.* 42).

Fig. 42.—Hexagonal plates of cystin.

It is insoluble in water, ether, and alcohol, but very soluble in ammonia and caustic alkalies.

A very good test for cystin is to boil some of its potash solution, dilute it with water, and add a little nitro-prusside of potash, when a beautiful violet colour is developed.

Leucin ($C_6H_{13}NO_2$) and *Tyrosin* ($C_9H_{11}NO_3$) occur in the urine in acute yellow atrophy of the liver. They are products of the pancreatic digestion, but are normally further oxidised into urea.

Leucin, precipitated spontaneously or obtained by evaporating an alcoholic extract of the urine, occurs in the form of yellowish brown balls. Tyrosin forms silky, colourless sheaves (*Fig.* 43) of needles. When slightly heated with a few drops of concentrated sulphuric acid it dissolves with a temporary deep red colour.

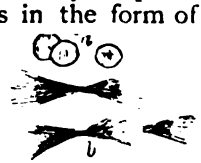

Fig. 43.—*a*, Balls of leucin which, with polarised light, show a dark cross; *b*, Sheaves of tyrosin.

According to Anderson both are frequently present in the urine of liver diseases.

Melanin is a pigment usually found in the urine of persons the subject of melanotic growths, but exceptionally at times

in others (SENATOR). It becomes black on exposure to the air. In a case of mine the urine was a dirty greenish brown colour, which gave the characteristic reaction of becoming perfectly black with solution of ferric chloride. With sodium nitro-prusside and caustic potash it became first violet and then a splendid claret colour; on adding acetic acid this changed to blue; other acids produced the same effect. With sodium nitro-prusside and ammonia it first became dull red then dull violet, and on adding acetic acid a splendid dark greenish blue was developed. There were no absorption bands, and neither indican, pyrocatechin, nor pyrocatechuic acid was present.

The test for it is solution of ferric chloride, with which it gives, as already stated, a perfectly black colour.

Indican ($C_8H_6NKSO_4$) is formed in the intestine by the pancreatic digestion, or by putrefactive change. It is derived from indol (C_8H_7N). By oxidation it forms indigo-blue.

It is increased in the urine in intestinal diseases, prolonged constipation, hernia, typhoid fever, cancer of the bowel, in Addison's disease, diabetes, Bright's disease, nervous diseases, peritonitis, cholera, fractures, osteomyelitis, etc. The largest quantity I have ever seen was in the very scanty urine of a hysterical patient. Ord has described a calculus formed from it.

The best test is to add to equal quantities of concentrated hydrochloric acid and urine, drop by drop, a solution of hydrochlorite of lime, and shake until a blue colour is developed; if the mixture is shaken up with chloroform the blue colouring matter is taken up by it and can be obtained as a deposit when the chloroform evaporates.

Hydrochinon ($C_6H_6O_2$) is the substance which gives the dark colour to urine in cases of carbolic acid poisoning. It is formed by oxidation.

C_6H_6O	+ O =	$C_6H_6O_2$
carbolic acid.	oxygen.	hydrochinon.

Pyrocatechin ($C_6H_6O_2$) is an isomer of hydrochinon, and also gives a dark colour to urine, especially where putrefaction has occurred.

Alcapton; Pyrocatechin; Protocatechuic, Uroleucic and *Uroxanthic Acids.*

Bödeker discovered a substance in the urine which darkens in the presence of alkalies, named by him alcapton.

This is said by Ebstein and Müller to be pyrocatechin, while Walter G. Smith thinks it protocatechuic acid.

Kirk believes it to be a compound body containing at least two components, which he has named uroleucic and uroxanthic acids.

In a case observed by Kraske, a man aged sixty-eight had been the subject of alcaptonuria since childhood. His urine contained pyrocatechin and hydrochinon-carbonic acid. Kraske found that the excretion of the latter was increased when tyrosin was mixed with his food.

Grape sugar ($C_6H_{12}O_6$) is present in traces (·03 per cent.) in normal urine, but in larger quantities in the urine of diabetes mellitus.

Milk sugar is said to be sometimes present in the urine of pregnant or nursing women.

Physiological traces of sugar are not recognisable by the ordinary tests.

Temporary or intermittent functional glycosuria occurs, but is rare.

In various serious organic diseases of the brain and spinal cord glycosuria may be occasionally met with.

The mode in which sugar is produced is not yet fully understood. Glycosuria occurs when the centre for the hepatic vaso-motor nerves in the floor of the fourth ventricle is punctured, or after section of the vaso-motor channels in the cord, or section of the vaso-motor nerves going to the liver. Glycosuria so induced may be stopped by section of the splanchnic nerves. Poisons which paralyse the vaso-motor nerves of the liver, *e.g.*, chloroform, ether, and chloral, produce the same effect.

The prevalent explanation of these facts is that the liver normally converts its glycogen into sugar in such quantities as can be oxidised in the tissues into water and carbonic acid; but when there is an excessive stimulus to the liver, it converts more glycogen into sugar than can be burnt off, and the excess appears in the urine. Modern observations make it probable that the conversion is a function of the activity of the liver cells on food principles, carbo-hydrates, peptone, and fat.

The ordinary clinical test for sugar is with *Fehling's* solution,* performed in the following manner.

* Martindale's formula :—(1,) Copper sulphate, 181 grains ; distilled water, to 6 ounces ; dissolve. (2,) Neutral potassium tartrate, 728 grains; caustic soda, 360 grains ; distilled water to 6 ounces ; dissolve. On mixing these two solutions in equal columns Fehling's solution is formed, of which 10 cc. will be decolorised and reduced by 0·05 grm. of diabetic sugar.

Boil about a drachm of the solution in a test tube, add an equal quantity of urine, boil again; if sugar is present the yellow suboxide of copper is thrown down.

Albumen causes a dirty purple precipitate, albumose turns Fehling rose pink, and uric acid, urates, kreatinin, glycuronic acid, aldehyde lactic acid, lactates and lactose, are all stated to reduce copper. The most certain and trustworthy test is fermentation by carefully washed yeast, in a test tube, or special tube inverted over mercury, and kept in a warm place; if as little as 0·1 per cent. is present it may be detected by a bubble of CO_2 collecting at the upper end of the tube.

Trommer's test.—The urine is rendered alkaline with liq. potassæ and copper sulphate solution, added drop by drop until the cupric oxide formed ceases to be dissolved. The mixture is then boiled, and reduction of the cupric oxide follows if sugar is present.

Moore's test.—The urine is treated with liq. potassæ and boiled, when it turns brown in the presence of sugar, but the reaction is neither certain nor delicate.

Johnson's test.—Put about half a drachm of a saturated solution of *Picric acid* in a test tube, add a few drops of dilute *Liq. potassæ* (1 to 10), boil the mixture, add an equal quantity of urine and boil again; if as much as one grain of sugar per ounce be present the liquid will become quite *opaque*, but a certain amount of reddish brown colouration takes place whether sugar be present or not.

Rubner's test.—To 10 cc. of urine add the same amount of concentrated solution of neutral acetate of lead, and filter. To the filtrate add ammonia drop by drop until a thick cheesy precipitate is formed. Heat cautiously to 80° C. (176° F.), when the precipitate will turn a rose red, and on further heating a coffee brown if sugar is present. This test is said to detect the presence of 0·25 per cent. of sugar.

Phenyl-hydrazin test (von Jaksch).—Two parts of hydrochlorate of phenyl-hydrazin (twice as much as will lie on the point of a knife) and three parts of acetate of soda are placed in a test tube with 6 to 8 cc. of urine. If the salts do not dissolve when the fluid is warmed a little water is added, and the test tube placed for twenty to thirty minutes in boiling water. After this it is taken out and put into a vessel containing cold water. If sugar is present a yellow crystalline precipitate forms at once, which is seen under the microscope to consist of yellow needles detached or arranged in

radiating clusters. This test is applicable to any morbid urine, and in the presence of albumen.

Other tests, such as indigo-carmine, safranin, and bismuth, exist, but they are not so commonly employed and have no special advantages.

The *quantitative estimation* of sugar is made with Fehling's solution. The necessary apparatus consists of a burette, a 100 cc. glass measure, a white porcelain dish, and a spirit lamp. Measure off 10 cc. of Fehling's solution with the 100 cc. glass, dilute with distilled water up to 50 cc., pour into dish and set on to boil. Measure 10 cc. of urine in the same way, and dilute up to 100 cc. (that is to ten volumes), and fill the burette with the diluted urine up to the zero mark. If the urine is turbid it should be filtered, and albumen must be removed by boiling. When the diluted Fehling has begun to boil the urine should be run in from the burette drop by drop, the operator stirring meanwhile, and from time to time removing the lamp so as to let the reduced copper settle, and to note the state of the fluid. When the blue colour has entirely disappeared, read off the quantity of diluted urine which has been required to effect this; this quantity contains exactly 0·05 grm. of sugar. Let us suppose that this was 10 cc. of dilute urine, then in order to find the percentage of sugar present we must say, if 10 cc. of dilute urine contains 0·05 grm. of sugar, how much will 100 cc. contain? Or as 10 : 100 :: 0·05 : x.

$$x = \frac{0{\cdot}05 \times 100}{10} = \frac{5}{10} = 0{\cdot}5.$$

But the urine was diluted to ten volumes, therefore this figure must be multiplied by ten, and the result is 5 per cent. As a rule it is important to determine not the percentage, but the actual quantity passed daily. This is easily done by reducing the number of ounces of urine to grains, multiplying by the amount per cent., and dividing by a hundred. For example, if 43,200 grains of urine have been passed in twenty-four hours, and a portion of this tested as above has been shown to contain 5 per cent. of sugar, then $\frac{43,200 \text{ by } 5}{100} = 2,160$ grs. of sugar passed in twenty-four hours.

A rough quantitative estimate may be made by fermentation; the urine is divided into two portions, which are placed side by side in a warm place and yeast added to one only. After some hours the specific gravity of both is taken, and,

according to Sir William Roberts, the quantity of sugar is represented by each unit of specific gravity lost by fermentation being equal to one grain of sugar per ounce. For example, the sp. gr. of the urine is 1040; two portions are placed side by side, and yeast added to No. 1 only. At the end of eight hours No. 2 has a specific gravity of 1042 (due to evaporation), and No. 1 is only 1006; the difference of 36 represents 36 grains of sugar per ounce, or 7·5 per cent.

The *araosaccharometer* is an instrument consisting of a flask with a long neck on which a scale is marked. The flask is filled with urine and ballasted with yeast until it sinks to zero on the scale; as fermentation takes place the flask rises, and the scale on the neck gives the amount of sugar.

The *polarimeter* affords a ready means of estimating the amount of sugar in urine previously precipitated with lead acetate and filtered. A series of estimations made by Dr. J. W. Russell showed that the results were slightly below those obtained by Fehling's solution or fermentation, but were sufficiently constant to prove that the instrument is trustworthy in practised hands; the personal equation forms too large a factor to make it suitable for the use of students.

Acetone (CH_3COCH_3) is met with in the urine of advanced cases of diabetes, of many acute febrile diseases, *e.g.*, measles, scarlatina, pneumonia, after the ingestion of alcohol (BULL), and even in the urine of healthy children (BAGINSKY).

Ralfe's modification of Lieben's iodoform test is performed by boiling a drachm of liq. potassæ with twenty grains of iodide of potassium in a test tube, and then upon the surface of this floating an equal quantity of urine. At the junction of the two fluids a ring of phosphates is formed, which in the presence of acetone becomes studded with yellow points of iodoform; unfortunately alcohol and lactic acid give the same reaction.

The best test is that devised by Le Nobel. Pour about an ounce of urine into a urine glass, add a drachm or two of a solution of nitro-prusside of sodium (5 grains to 1 ounce), and a few drops of strong *ammonia*. After standing a few minutes a rose violet colour is developed, which, if much acetone is present, will require diluting with water to bring out the brilliancy of its colour.

Acetone is probably formed in the urine by the breaking up of aceto-acetic acid into acetone and carbon dioxide.

$$CH_3,CO,CH_2,COOH = CH_3,CO,CH_3, + CO_2$$

Aceto-acetic acid or *diacetic acid* ($CH_3,CO,CH_2,COOH$) is present in the urine of diabetes, and gives a red coloration with *ferric chloride solution*, which disappears on heating. This *ferric chloride reaction* was at one time thought to be a test for acetone. According to Le Nobel the same reaction is given by β-oxybutyric acid, sulpho-cyanogen, acetic and formic acid compounds, only differing by not disappearing on the application of heat.

The large number of substances which give this reaction accounts for its being so commonly met with, as in coma, chronic Bright's disease, perityphlitis, strangulated hernia, after minor surgical operations, and in sulphuric acid poisoning (WINDLE).

Bile pigment or *bilirubin* ($C_{32}H_{36}N_4O_6$) is present in the urine in cases of jaundice, sometimes before any change is to be observed in the skin or conjunctivæ. It colours the urine deep yellow, mahogany brown, or olive green. The last colour is due to partial oxidation of the bilirubin to *biliverdin* ($C_{32}H_{36}N_4O_8$). Bile-stained urines may turn *grass green* from this change, which only takes place when the urine is undergoing decomposition.

The peculiar colour of bile-stained urine can be usually recognised by the eye, even when only a small quantity of the pigment is present ; but some dark urines look very much as if they contained a large quantity of bile pigment until they are well diluted with water.

The best way of testing for bile pigment is to dilute a couple of ounces of the urine to the colour of sherry in a urine glass, add a drachm or two of strong *nitric acid* containing some *nitrous acid* (such nitric acid has a yellow colour), or weak liq. iodi (1 to 10 of water); if bile pigment be present a grass green colour is developed. Sometimes one and sometimes the other of these tests gives the best result.

The method by dilution in a urine glass is recommended as giving much better results than the plan ordinarily followed of making a play of colours by mixing a drop of urine with a drop of nitric acid on a white porcelain dish.

Bile acids, glycocholic ($C_{26}H_{43}NO_6$) and taurocholic ($C_{26}H_{45}NSO_7$) acids are often present in the urine of jaundice. The various tests for these acids are unsatisfactory. Pettenkofer's well known reaction with sugar and sulphuric acid cannot be obtained when applied to the urine directly, but the acids must be first isolated.

The following test is recommended by Hay. Sprinkle a little *precipitated sulphur* on the surface of the urine. If bile acids are present the grains of sulphur *float*, instead of sinking as they otherwise do; but it does not appear to be of any value.

Oliver's test consists of powdered peptone 2 grms.; salicylic acid 0·25 grm.; acetic acid 30 drops; distilled water 240 grms. To 4 cc. of the solution add twenty drops of the urine to be tested; if bile acids are present an opalescence is produced, varying in intensity with their quantity.

Fat or oil globules may be found in the urine after the passage of a catheter, and are of course derived from the oil used on the instrument; they are met with also in phthisis, pyæmia, long standing suppuration, and phosphorous poisoning, from fatty degeneration of pus, or of renal or vesical epithelium; but in all these conditions they are present only in quantities recognisable by the microscope.

In *chyluria* the urine is milky from admixture of fat. This condition occurs sometimes in pregnancy and lactation. Mr. Frost, of Yardley, a year or two ago brought me the urine of a young unmarried girl, who, having become pregnant, had compressed her abdomen so much in order to conceal her condition as to cause œdema of the legs, thighs, vulva, and lower part of the abdomen. After her confinement the urine became milky and remained so for some days; it contained fatty granules, cholesterin, and albumen, but no sugar.

Francotti has described a somewhat similar case in which a woman who had never resided in the tropics passed chylous urine in each pregnancy. With rest it diminished or disappeared, recurring on going about.

In both these cases there was probably some rupture of dilated lymphatics with escape of lymph or chyle into the urine.

Rossbach has published a case of a young girl with mitral insufficiency who passed milky urine both by day and by night. The daily quantity of fat excreted varied from 1·5 to 10 grammes. The urine also contained albumen. The patient had diminished liver dulness, and he suggests that it is possible the condition depended in some way upon disease of the liver.

Endemic chyluria occurs commonly in India, China, and the Straits in persons whose blood is infested by the parasitic nematode, *filaria sanguinis hominis*. Chyluria is caused when

the lymphatics get obstructed through the impaction of abortive ova in the ducts (MANSON).

Fatty acids, *e.g.*, butyric acid, are sometimes present in the urine.

Cholesterin ($C_{24}H_{44}O$) is met with in chylous urine, in fatty degeneration of the kidney, in diabetes, jaundice, and in the urine of epilepsy treated with potassium bromide (PÖHL), while it enters into the constitution of certain urinary calculi.

Its crystals can be recognised under the microscope as large thin rhomboidal colourless plates (*Fig.* 44). With iodine and sulphuric acid they turn to deep blue or violet colour.

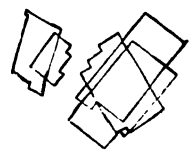

Fig. 44.—Crystals or plates of cholesterin.

A further test may be made by dissolving the cholesterin with chloroform in a test tube, adding concentrated sulphuric acid and shaking for some minutes; the chloroform in the presence of the slightest trace of cholesterin becomes citron yellow, with a larger quantity, blood red or purple. On the addition of water to the chloroform solution it becomes quickly blue, then green, and finally yellow. With glacial acetic acid the violet solution shows a green fluorescence.

Albumen.—By albumen is meant serum albumen, with its acid and alkaline modifications, and serum globulin (paraglobulin).

It must be borne in mind that the clinical examination of the urine is not a scientific enquiry, but a practical method founded upon empirical as well as upon scientific data. There are albuminoid bodies in the urine which have no known clinical significance, and these can only embarrass the practitioner who is looking for a sign to which he attributes a significance based upon a purely empirical foundation. Posner has proved that a minute amount of serum albumen is a constant constituent of normal urine, so that if we could obtain a very delicate test for albumen it would be actually misleading to us.

I have defined albuminuria as *the presence in the urine of a substance which is coagulable by heat or precipitated by neutralisation.* This definition includes serum albumen, with its modifications, and serum globulin, while it excludes a variety of albuminous substances which are sometimes present in urine, but concerning whose pathological relationships we know very little.

In order to find minute traces of albumen the following method and precautions should be carefully adhered to. Albumen is most constantly present in the urine passed in the forenoon, so that it is best to obtain a specimen passed at that time if possible.

Putrid urine is unfit for detecting traces of albumen, and turbid urine, unless the turbidity be due to urates which will disappear on heating, should be filtered.

Fill a test tube two-thirds full of urine, hold it by the lower end and boil the upper half *well* over a spirit lamp, then acidulate with two or three drops of *dilute acetic acid.* If there is any difficulty in recognising a cloud, hold the tube against a shaded back-ground with the light falling from above, when the faintest haze will be apparent by contrast with the layer of unboiled clear fluid below. If the room is badly lighted, or the examination is made by artificial light, a very faint haze may escape detection.

This haze indicates the presence of serum albumen or serum globulin. There is no single operation by which these can be differentiated. If it is desired to do so a portion of the urine must be saturated with common salt or with magnesium sulphate and filtered. By this means the globulin is precipitated, so that if a urine before precipitation gave a cloud on boiling and acidulating, but none afterwards, we should be justified in concluding that the albuminous body was serum globulin. But globulin very rarely occurs by itself, and when it does it has not been proved to have any significance, though Hermann has stated that he found only globulin in a case of eclampsia, while in the nephritis of pregnancy he found serum albumen. It has been repeatedly suggested that in various forms of "functional" albuminuria, the albuminous body is globulin, but this statement has hitherto in all cases been proved to be erroneous; there can be no doubt that the presence of globulin unaccompanied by albumen is very exceptional and has at present no definite meaning.

Noel Paton has devised a simple and fairly accurate procedure for the quantitative determination of serum-albumen and serum-globulin based on Esbach's method.

It may be contended that it would be better to have a test which does not throw down globulin, and this may be readily granted, but there is no test which is perfect. This trifling imperfection will never lead any one astray who bears in mind

that the discovery of albuminuria is not a fact "per se" of definite pathognomonic significance.

It has been objected that urine which contains oxalate of lime gives a reaction resembling albumen with this test. This is true if urine is saturated with oxalic acid, filtered and then tested, but the haze is a *very* faint one, and it is not true in my experience of oxaluria as observed clinically.

One observer has stated that mucin gives a cloud resembling albumen, but this is not the case. On adding acetic acid mucin coagulates in tiny filaments easily distinguished from albumen.

Heller's test, with *cold nitric acid*, is a very good plan. It is performed by pouring a few drops of nitric acid into a test tube and then floating half a drachm of urine by means of a pipette on its surface. Where the liquids come in contact a cloud forms when albumen is present.

The objections to this method are: (1,) That it is not so delicate as the heat and acetic acid plan, though, like that, it throws down globulin; (2,) That the reaction is simulated in the urine of patients taking copaiba, cubebs or salicylic acid; (3,) That nitric acid is hurtful to one's fingers, clothes and carpets, when it gets spilt, as in the course of daily use it is certain to be sometimes; (4,) That it gives a cloud with uric acid, and that urea may crystallise out.

The use of *picric acid* has been strongly advocated of late years. It is recommended to employ a double saturated solution of common salt and picric acid, which is heavier than most urines, and it is then used like cold nitric acid as just described, a cloud forming where the two liquids come in contact.

The objections are: (1,) That this reaction occurs with *albumose*, an albuminous body of no known pathological significance, which is frequently present in urine; with alkaloids, such as quinine, and with mucin.

The cloud given by albumose and alkaloids disappears on heating; but if the spirit lamp is to be employed in every case the test loses its principal advantage of simplicity. Unfortunately the fallacy from mucin cannot be got rid of except by testing separately for mucin. (2,) Picric acid is not so delicate as either of the above described methods. There is some conflict of testimony on this head, but this is my experience, and it is supported by Roberts, Lauder Brunton, Harris, and Stirling.

Ferrocyanide of potassium and *acetic acid* give unsatisfactory results in the examination of urine, as they throw down albumose, as well as albumen proper.

Tanret's test, *potassio-mercuric iodide*, also throws down albumose as well as albumen, the cloud produced by the former substance not disappearing on heating.

Tungstate of soda possesses the same fallacious power, and also gives a cloud with mucin.

It is unnecessary to go further through the various tests which have been recommended. It is possible that individuals may find themselves able to get better results with one test than another; but the three methods described fully, namely, boiling and acetic acid, cold nitric acid and picric acid, are those which have received the support of the best authorities; all others are for various reasons useless or fallacious.

When a *quantitative analysis* is required the most accurate way is to boil a known quantity of urine, acidulate it, and collect it on a weighed filter paper, dry it over sulphuric acid in a bell jar, and weigh it carefully, deducting the weight of the paper. But this is a method unsuited to the needs of practitioners.

Fig. 45.

A very easy and fairly accurate method has been invented by Esbach. The only apparatus required is a specially graduated tube (*Fig.* 45). The urine, diluted with one or more volumes of water, is poured into this tube up to the line marked U, and the albumen is precipitated by a solution of *picric* and *citric acids* (ten grammes of picric acid, and twenty grammes of citric acid, dissolved in eight hundred or nine hundred ccm. of boiling water, and enough water added to make up one litre), the tube being then allowed to stand a few hours when the result is read off as a percentage, and corrected according to the number of volumes of water added.

When we wish to estimate the amount of albumen by either method, it is necessary to make use of a sample of the whole twenty-four hours' urine in order to give the observation any value, as the proportion of albumen varies very much at different times of the day and night.

Albumose has no known pathological significance, but is met with in many acute diseases; it was formerly called *peptone*, but all modern observers are agreed that it is more

properly described as albumose, being thrown down by ammonium sulphate (VON NOORDEN). The test for it is that it gives a *pink* colour with Fehling's solution in the cold; it is better to dilute the reagent with an equal quantity of distilled water.

Mucin is commonly present in the urine of even healthy persons, causing a light flocculent cloud which gradually settles to the bottom of the vessel. In catarrh of the urinary passages it is much increased and mixed with pus.

It is precipitated by acetic acid in the form of fine filaments, and by alcohol, citric acid, picric acid, tungstate of soda, etc. After boiling with hydrochloric acid, mucin reduces cupric oxide like sugar.

Blood.—The presence of blood in the urine is a symptom common to a number of pathological conditions, differing essentially in their seat, nature, and relationships. It may appear in a corpuscular or non-corpuscular form; the latter is called hæmoglobinuria.

In paroxysmal hæmoglobinuria the primary cause is cold, acting on the blood in the vessels of peripheral parts, *e.g.*, hands, feet, ears and nose, where the circulation is sluggish. There is a nervous factor co-operating which probably acts by slowing the circulation in certain parts, and it is particularly liable to come on in predisposed persons after muscular exertion.

Blood can generally be recognised in the urine by the eye, even when present in small quantities. It is characteristic of blood that its solutions are dichroic, appearing red by reflected and green by transmitted light. But acid urine soon changes the bright red colour into a dirty brown (methæmoglobin), so that urine which has remained in the bladder mixed with blood is smoky brown or porter-coloured, according to the amount of blood present.

The *microscope* is undoubtedly the best means of detecting corpuscular blood in the urine. A drop of urine should be taken up by a pipette and placed on a glass slide, covered with a thin cover-glass, and examined with a lens of at least two hundred and fifty diameters magnifying power.

If traces of blood only are present the lowest stratum of urine should be examined after standing some time. The corpuscles undergo many changes, swelling up so as to lose their bi-concave form, or shedding their hæmoglobin, by which they alter in shape, appear vacuolated, and ultimately colourless.

(*Fig.* 46.) Such colourless discs may possibly be confounded with discoid oxalates and torulæ, but both these are smaller, while the latter contain bright nuclei and are generally oval.

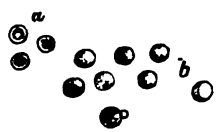

Fig. 46. Blood discs: *a*, Discs preserving their bi-concave shape; *b*, Discs swollen by imbibition of water, shedding their hæmoglobin and becoming colourless.

The Guaiacum test.—This depends upon the ozone-carrying power of hæmoglobin. It is best performed by dissolving one or two drops of fresh tincture of *guaiacum* in about half a drachm of ozonic ether, which is a solution of *peroxide of hydrogen* in *sulphuric ether*, and then adding about a drachm of urine and shaking the mixture. If hæmoglobin be present a blue colour appears. Another method is to dip strips of blotting-paper in the tincture and dry them. These are used by touching them with a drop of urine and a drop of ozonic ether successively. *Turpentine* which has been exposed to the air always contains ozone, and may be substituted for ozonic ether but cannot be depended upon so well. Unfortunately this test is not quite perfect. The urine of patients containing iodide of potassium gives a blue colour although no blood be present, while I have often observed that corpuscles are to be seen with the microscope when the chemical report says "no blood reaction." With respect to this want of delicacy two cautions may be given. The guaiacum tincture should not be kept longer than two months: and, secondly, the urine to be tested should be drawn up with a pipette from the lower stratum, just as it would be for microscopical observation, as the corpuscles naturally sink to the bottom of the glass.

It is stated that fibrin possesses the power of decomposing peroxide of hydrogen, giving a blue colour with the guaiacum test. I have not been able to obtain this result with well-washed fibrin, but in any case fibrin is not likely to be met with in urine apart from hæmaturia.

The *spectroscopic* examination of blood in solution is easy, and may be made by holding the vessel containing the urine between the source of light and an ordinary pocket spectroscope applied to the eye, when two dark bands will be visible between Fraunhofer's lines D and E in the yellow and green of the spectrum; if the colouring matter is converted into methæmoglobin, a band in red will appear in addition to the other two. When the blood is present in an insoluble state the urine must be filtered, and the filter paper with the deposit

upon it digested in *alcohol* and *ammonia*. This fluid should be examined as in the other case, but if little blood be present the faintest possible shadow in the orange of the spectrum may alone be visible; on adding *ammonium sulphide* to the fluid the two bands will show themselves, but disappear when the fluid is shaken with air, to reappear on standing.

Hæmatoporphyrin is a beautiful red pigment derived from the blood, said to be present in traces in normal urine, but found in excess in many acute and chronic diseases, but especially after taking large doses of sulphonal. It may be thrown down by treating the urine with excess of caustic potash or caustic soda; the precipitate should be washed with distilled water, and treated with acidulated alcohol when an almost pure solution of hæmatoporphyrin may be obtained (SALKOWSKI, COPEMAN, GARROD).

Pus may be found in the urine whenever inflammation affects any part of the urinary tract, but it is most commonly met with in catarrh of the urethra (*gonorrhœa*), of the bladder (*cystitis*), or catarrh of the pelvis of the kidney (*pyelitis*). In the second condition the urine is generally alkaline, and triple phosphates are found with the pus; in the latter the urine is generally acid and the deposit commonly contains oxalates. Pus is best detected by the microscope (*Fig.* 47), the round leucocyte-like cells are easily recognised; by adding acetic acid they become clear and show two or more nuclei; sometimes they are opaque from infiltration with micro-organisms, when acetic acid will fail to clear them.

Fig. 47. *a*, Pus corpuscles; *b*, cleared by acetic acid, showing two, three, and four nuclei.

When pus is present in quantity it effervesces with *ozonic ether*, but this is not a delicate reaction. On the addition of *liq. potassæ* the liquor puris becomes ropy, even when a small quantity is present.

Pus when present in quantity in the urine forms a cream-coloured deposit, which is not readily diffused into the supernatant fluid.

Casts are moulds of the tubules of the kidney and are of three kinds: (1,) *Blood* casts, formed of red corpuscles stuck together by fibrin; (2,) *Hyaline* casts, originating in various ways: (*a*,) From fibrin; (*b*,) From a protoplasmic exudation from the renal epithelium in the early irritative stages of acute nephritis or in chronic inflammation; (*c*,) From the colloid degeneration of desquamated epithelial cells. The second is

probably the most common type; such casts are slender, while the third kind are broad and have the same meaning as epithelial casts; (3,) *Epithelial* casts, formed either by the packing together of desquamated and fatty epithelium, or by masses of round cells derived by proliferation from the epithelium of the

Fig. 48. *a*, Blood cast: *b*, Epithelial cast composed of small round cells: *c*, Epithelial cast formed of desquamated and fatty epithelium; *d*, Granular hyaline cast; *e*, Hyalo-epithelial cast.

tubules, indicate a high degree of active inflammation of the renal parenchyma (*Figs.* 48 and 49).

To find casts use a half-inch objective, with a good light. Take up a drop of the deposit or lowest stratum of the urine with a fine pipette, and place six drops on as many slides. (Very suitable pipettes are sold as "biological pipettes," made of thick glass with a bore of about one-sixteenth of an inch.) Cover each drop with a thin cover-glass, and examine the slides in succession; if no casts are found on any of them the result may be regarded as fairly indicating their absence from that specimen of urine.

In acute Bright's disease casts are very abundant. Out of sixty-seven observations only nine were negative, and these were all at the termination of the cases when they were nearly cured, though it is noteworthy that albuminuria still persisted.

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In chronic Bright's disease associated with dropsy, where there was a recent history of acute nephritis, they were absent in only four out of ninety-five observations.

In chronic Bright's disease with little or no dropsy they were also very constant, being present in sixty-eight out of seventy-seven observations; but they were not abundant. In cases of contracting kidney seen in the out-patient room, and diagnosed as such from other signs and symptoms, casts were present in sixteen out of twenty-five observations.

Epithelium of various kinds occurs in the urine. Large squamous cells from the vagina and urethra of women, and the bladder of both sexes, are common. The epithelium from the male urethra is columnar. Pear-shaped or tailed cells may come from Cowper's glands, Littré's glands, the prostate, the ureter, and pelvis of the kidney.

Small round cells, derived by proliferation from the renal epithelium, may be seen in acute Bright's disease. (*Figs.* 49 and 50.)

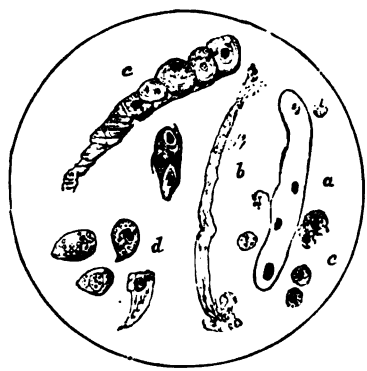

Fig. 49. *a*, Slender hyaline cast; *b*, Mucous cylinder; *c*, Hyaline and epithelial cast; *d*, Pear-shaped epithelial cells from pelvis of kidney; *e*, Epithelium from tubules.

It is not always possible to say whence given cells are derived; they often have undergone fatty degeneration or infiltration by microbes, or are broken up into fragments.

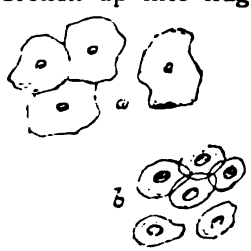

Fig. 50. *a*, Large squamous epithelium from vagina; *b*, Epithelium from bladder.

Epithelial cells must be looked for with a good quarter-inch glass.

Micro-organisms are not present in normal urine, as it may be kept for months in a warm place without undergoing any change; but Kannenberg states that he has found spheroid and rod-shaped forms in the urine of healthy persons, though much more abundantly in all acute diseases. Lustgarten and Mannaberg also found organisms in the urine of healthy persons, for the urethral mucus of eight healthy persons contained ten different kinds of microbes (in four cases bacilli and in six micrococci). Of these ten

varieties, two were especially notable, one being a bacillus giving the staining reactions of the *bacillus tuberculosis*, the other a micrococcus indistinguishable from the *gonococcus* or microbe of gonorrhœa. They found that it was necessary to take the precaution of drawing off the urine by a catheter in order to obtain a secretion which on cultivation was free from organisms.

They found numerous *streptococci* (organisms arranged in chains) in the carefully drawn off urine of three cases of acute Bright's disease, which disappeared on the decline of the disease. They did not succeed in obtaining a pure culture of these organisms.

Undoubtedly many organisms find their way into the urine after it has left the body; *torulæ* are not uncommon, especially in urine containing sugar. These *torulæ* are the sporules of the common moulds (*penicillium glaucum* and *aspergillus niger*), and of the yeast plant (*saccharomyces cerevisiæ*). Putrid urine swarms with bacteria, of which the best known is *bacterium termo*. The ammoniacal decomposition of urine is said to be due to the action of a minute spherical bacterium called by Cohn *micrococcus ureæ*.

In morbid conditions of the urinary tract, as well as in many specific diseases, organisms are found in the freshly passed urine which do not give rise to any chemical changes in it; one of the earliest known was *sarcina ventriculi*, which appears in the urine in certain cases of vesical catarrh, but seems to be invariably introduced by surgical interference (catheters); it may persist for years and does no harm (FINLAYSON). Roberts has described three cases of *bacteruria* associated with bladder troubles.

Tubercle bacilli have been found in the urine in tubercular diseases of the urinary organs, and of the epididymis (ROSENSTEIN). Bouchard found micro-organisms in the urine of typhoid fever, puerperal fever, measles, erysipelas, dysentery, osteomyelitis, diphtheria and phthisis.

Berlioz found the typhoid bacillus in the urine of two out of fourteen cases, in one instance on the twentieth day of the disease. In two cases of pneumonia and five of erysipelas his results were negative.

In animals inoculated with charbon he observed the passage of bacteria into the urine in two cases accompanied by hæmoglobin. The passage was found to be facilitated by cantharidin poisoning, by which the kidneys were irritated. He also

observed the passage into the urine of the *micrococcus tetragonus*, the *bacillus pyocyaneus*, and the *pneumococcus* of Fraenkel. He believes that these appearances always denote a morbid localisation in the urinary apparatus.

Schweiger found that organisms injected into the renal vein or artery soon appeared in the urine, and conversely when injected into the pelvis of the kidney could be found by cultivation in the blood. He attempted to determine where the passage takes place, but was unable to detect them *in transitu.*

In many conditions micro-organisms have been observed in the kidneys *post mortem* when they have not been found in the urine, *e.g.*, *micrococcus diphtheriæ*, the micrococcus of *ulcerative endocarditis*, *microsporon septicum*, Friedländer's *pneumococcus*, etc.

The method of examining urine for micro-organisms is the following: Place a drop of the deposit, or of the urine on a cover-glass which has been cleansed with nitric acid and distilled water. Place another cover-glass upon the drop and press the two together, then separate them by sliding one over the other. Allow the films of fluid to dry, then holding the covers with a pair of forceps pass each two or three times quickly through the flame of a spirit lamp or Bunsen's burner. Stain them with methyl violet solution.

Saturated alcoholic solution of methyl voilet	11	parts.
Aniline water	110	„
Absolute alcohol	10	„

They may be left in this solution several hours. Wash with alcohol for three minutes, then in a solution of ten parts iodine, twenty parts iodide of potassium, and three thousand parts of distilled water, until the dark blue violet is replaced by a dark purple red. Wash in alcohol till most of the colour is removed. The covers may be mounted at once on glass slides with a little Canada balsam.

This is Gram's method as given by Woodhead and Hare, to whose book readers are referred who want information about special stains and methods of cultivation.

The accompanying woodcut shows various forms of micro-organisms (*Fig.* 51).

Ferments are stated to be present in normal urine. *Trypsin*, the proteolytic ferment of the pancreas which occurs in normal urine, is said by Mya and Belfanti to be replaced by pepsin in Bright's disease.

Holvotschiner and Breusing have found that there is an amylolytic ferment present which is capable of converting starch into erythro- and achröo-dextrines, but not farther according to the second of these two observers.

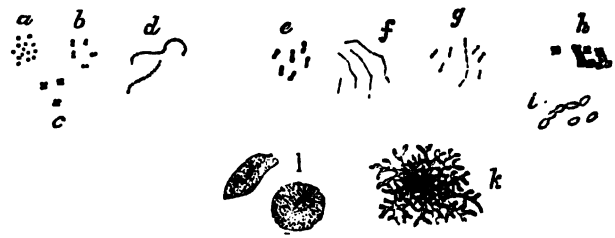

Fig. 61. *a*, Micrococci; *b*, Diplococci; *c*, Cocci in fours; *d*, Streptococci, or cocci in chains; *e*, Bacterium termo; *f*, Bacillus subtilis; *g*, Bacillus tuberculosis; *h*, Sarcinæ ventriculi; *i*, Torulæ; *k*, Mycelium; *l*, Zoöglœa.

Béchamp's "nephrozymose," an albuminous body in urine with the power of converting starch into sugar, is said by Leube to be a compound of albumen with some amylolytic ferment.

There is no reason to think that the amylolytic ferment, even if capable of converting starch into sugar, is ever responsible for the occurrence of paradoxical glycosuria, as there is no carbo-hydrate in the urine upon which it could exercise its powers.

Ptomaines of both the alpha and beta series have been found in the urine, not only as already mentioned in association with cystin, but in exophthalmic goitre, and other diseases (BOINET, SILBERT, ROOS), and it is probable that the toxic character of so many morbid urines is due to the presence of these substances (BOUCHARD, LÉPINE); for the methods of detecting these poisons the chemical text books must be consulted, as they are too complicated for description in a work of this kind.

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SECTION III.—DIABETES.

CHAPTER XVI.

DIABETES MELLITUS.

DIABETES Mellitus is essentially one of those rarer diseases which can only be effectively studied, at least in this country, by those who reside in great centres of population and have the extensive practice of a large hospital from which to draw their cases, as well as the opportunities of treating numerous individuals suffering from this malady under those conditions of control which can rarely be obtained except in the wards of such an institution. In the following lectures it is my purpose to describe this disease in the light of the clinical and pathological experience acquired in many years of hospital study, and I shall try to infuse into them as much as is possible of the results of my bedside observations and *post mortem* examinations, testing all theories by these standards. There is probably no disease which is so overweighted by theoretical considerations derived from an overwhelming amount of physiological experiment. But it is absolutely necessary to keep such physiological considerations in their proper place, using them only for the purpose of elucidating the facts of disease, not substituting one for the other, as if a frog with its spinal cord divided, or a rabbit with its medulla injured were really and truly a case of diabetes.

HISTORY.

Hirsch can hardly be held to be free from a tendency to exaggeration when he says that the history of diabetes goes back to the most remote antiquity. He is doubtless right in quoting the passages from the *Ayur Veda* in proof that the disease was known long ago to the Hindoos, but this *Veda* was certainly not written till the sixth century of our era, and is supposed to have been in great part a copy of Greek medicine transmitted through Arab sources. It is, however, very

noteworthy that in these quotations the urine is said to be *sweet*, and in a Cingalese treatise of the fifteenth century the disease is described as "Madu mehe" or "honey urine," though no reference to this very singular peculiarity can be traced among European writers until two centuries later. No mention of diabetes can be discovered in the writings of Hippocrates; and though Celsus described a disease attended by polyuria, wasting and bodily illness, the term diabetes was first used by Aretæus (A.D. *circa* 150). Galen wrote on the disease at some length. But neither of these authors referred to the *sweetness* of the urine, and this important fact remained undescribed until it was noted by Willis (1679). Sydenham, contemporary with Willis, wrote a good account of diabetes in which he drew attention to the importance of abstinence from vegetable food. "Let the patient," he wrote, "eat food of easy digestion, such as veal, mutton, and the like, and *abstain from all sorts of fruit and garden stuff*."

A century later Dobson (1776) evaporated two quarts of diabetic urine and obtained a cake which weighed 4 oz. 2 dr. 2 scr. This cake "smelt sweet, like brown sugar, and could not be distinguished from sugar, exeept that the sweetness left a slight sense of coolness on the palate," probably due to the presence of a certain proportion of sodium chloride.

Cullen, in the first edition of his "Practice of Physic" (1784), wrote that the urine in diabetes contained a considerable quantity of a saccharine matter which seemed to be exactly of the nature of sugar. So impressed was he with this discovery that he would hardly admit the existence of a non-saccharine variety (diabetes insipidus), though he thought he had seen a case.

The publication of Rollo's excellent cases (1797) marks an era in the history of this disease, because of his powerful advocacy of meat diet, and the success which attended the method of treatment he employed, so that he may be said to have established the foundation of our modern practice.

Latham (1810) went a step farther in recognising two types of diabetes, one *saccharine*, and the other *serous*, and combined Rollo's animal diet with such excellent remedies as opium, iron, and alkalies.

Gregory, in the appendix to his edition of Cullen's "Practice of Physic" (1829), described two forms, D. insipidus and D. mellitus. He wrote slightingly of Rollo's treatment, which seems to have suffered a check in its popularity, when it

became known that in very many cases it failed to cure the disease. Nevertheless this method held its ground until modified by Bouchardat (1841), who introduced gluten bread.

In 1848 Claude Bernard discovered sugar in the liver after death, and in 1859 he proved that this sugar existed in the liver during life in the form of glycogen. He believed that glycogen was converted into sugar by the action of a diastatic ferment contained in the blood. In 1858 Pavy proved that the formation of sugar in the liver in such large quantities was a *post mortem* phenomenon, and he disputed the conversion of glycogen into sugar at all as a physiological process, suggesting that it really left the liver in some other form, such as fat. The great discovery of Bernard that puncture of the floor of the fourth ventricle was followed by glycosuria, gave, however, a possible explanation of the pathology of diabetes, though this has been greatly diminished in value by the subsequent experiments which have shown that lesions of many parts of the nervous system are followed by the same phenomenon. The present position of the problem cannot be described adequately by continuing the historical method. In order to render it as clear as possible the physiology of glycosuria will be explained at length in the next section, while the etiology, morbid anatomy, and pathology of diabetes will be dealt with separately in subsequent pages.

THE PHYSIOLOGY OF GLYCOSURIA.

By glycosuria is understood the presence in the urine of glucose ($C_6H_{12}O_6$). That this substance is present in small quantities in normal urine has been long known, but in such small amount (about 0·5 per 1000) that it can only be demonstrated by the usual tests after concentrating a large bulk of urine. Wedenski has utilised Baumann's discovery, that benzoyl chloride forms insoluble compounds with carbohydrates, in order to demonstrate the existence of this physiological glycosuria. G. S. Johnson has disputed its occurrence, relying upon the negative result of the phenyl-hydrazin test, but he uses this test in a way which is not recommended by its originator, and is, in my experience, quite untrustworthy.

The *glucose* found in the urine, whether normally or under pathological conditions, is as a rule grape sugar (dextrose).

Lævulose or intestine sugar is stated to occur rarely, but is not distinguished from it by the ordinary tests. *Inosite* or muscle sugar is an isomer of glucose, but occurs very rarely in

the urine, and is of little practical importance; it does not reduce cupric salts.

Lactose ($C_{12}H_{22}O_{11}$) or milk sugar, is a *sucrose*, but it is sometimes present in the urine during pregnancy or lactation, and reduces copper salts, though less actively than glucose, so that its presence is liable to be mistaken for that of the latter.

The reduction of copper in Fehling's or Trommer's test is so very generally regarded clinically as proof of glycosuria that great interest attaches to the discovery of the not uncommon occurrence of a non-saccharine body in the urine which possesses this power in a high degree. Schmiedeberg and Meyer have shown that this substance is glycuronic acid. It is found in the urine after the administration of various drugs, chloral hydrate, croton chloral, camphor, phenacetin, morphia, chloroform, and curare. Ashdown met with it in the urine of a young man, aged twenty-four, who enjoyed perfect health, or at least a complete sense of well-being. Glycuronic acid ($C_6H_{10}O_7$) occurs in the urine in combination with urea, but the nature of the compound has not been definitely determined. Ashdown recommended that in all doubtful cases the urine should be fermented.

Glucose is regarded by modern chemists as an aldehyde or ketone of a hexatomic alcohol ($C_6H_8(OH)_6$), which by oxidation yields ($C_6H_{12}O_6$) or glucose. This unit is called a monosaccharid; if two such units are linked together we get a di-saccharid, and this is the composition of the sucroses, *e.g.*, cane sugar, milk sugar, maltose, etc. The products of the actions of salivary and pancreatic diastase on starch are probably maltose, but by the time this reaches the portal vein it has become glucose. When more than two such units are linked together the result is a polysaccharid, *e.g.*, dextrine, starch, and glycogen. We know that the action of certain ferments can break up the polysaccharid into its components, and the liver, muscles, etc., possess a double power, being able to build up glycogen out of glucose, or to break up glycogen to form glucose.

Glycogen ($6(C_6H_{10}O_5) + H_2O$) is formed in the liver cells in the form of amorphous granules collected around their nuclei, and is irregularly distributed through the liver. It is soluble in water, but not readily diffusible, and gives a deep red colour with iodine solution. With diastatic ferments, or when boiled with a mineral acid, it forms grape sugar. The following directions for its preparation are taken from Lan-

dois and Stirling: "Let a rabbit have a hearty meal and kill it three or four hours thereafter. The liver is removed immediately after death; it is cut into fine pieces, plunged into boiling water and boiled for some time in order to obtain a watery extract of the liver cells. To the cold filtrate (of this extract) are added alternately dilute hydrochloric acid and potassio-mercuric iodide as long as a precipitate occurs. The albuminates or proteids are precipitated by the iodine compound in the presence of free HCl. It is then filtered, when, a clear opalescent fluid, containing the glycogen in solution, is obtained. The glycogen is precipitated from the filtrate, as a white amorphous powder, on adding an excess of 70 to 80 per cent., alcohol. The precipitate is washed with 60 per cent., and afterwards with 95 per cent., alcohol, then with ether, and lastly with absolute alcohol; it is dried over sulphuric acid and weighed" (BRÜCKE).

The quantity in the liver is increased by adding starch, milk, fruit, or cane sugar, alkalies (DUFOUR), glycerine, or inosite to the food, while it is diminished by a purely albuminous or purely fatty diet, and disappears during hunger. It is also diminished by cold and violent muscular exercise (KÜLZ), and by ligature of the bile duct (WICKHAM LEGG, VON WITTICH).

When rabbits are kept without food for six days, it is at least four hours after feeding before glycogen is found in their livers (KÜLZ). It is noteworthy that in diabetes an increase of sugar can be noted in from 1 to 1½ hours after the use of starchy food.

Glycogen is not a product peculiar to the liver; in fœtal life it is found in all the tissues of the body, and in the adult occurs in muscle, cartilage, the colourless blood corpuscles, the testicles, etc.

It can be formed directly from sugar in muscle, and by injecting syrup into the circulation a direct conversion of sugar into glycogen can be proved to take place.

As has been already stated, under physiological conditions glycogen is formed in the liver cells from the products of digestion of starchy and saccharine food.

It is probable that in health the glycogen is very gradually converted into sugar, in very small quantities (LANDOIS), as it is found to diminish during hunger (PAVY), exercise and exposure to cold. The sugar so produced passes into the circulation where it is rapidly used up as it passes through the systemic capillaries.

But whenever there is derangement of the hepatic circulation, permitting a greater afflux of arterial blood to the liver, the formation of sugar from glycogen is increased, and sugar in larger quantities passes into the general circulation.

This sugar production is now thought to be a product of the vital activity of the liver cells (PATON) under the stimulus of the excito-secretory nerve, or according to Pavy, it results from the contact of *arterial* blood.

The vascular derangement which permits this great afflux of arterial blood to the liver is assumed by Pavy to be a vaso-motor paralysis of the splanchnic area, in consequence of which the blood reaches the portal vein without becoming deoxygenised.

Kühne and Heynsius have suggested that glycocholic acid may split up into urea and glucose, and they found that the introduction of glycocin ($C_2H_5NO_2$, or sugar of gelatine, a constituent of bile) into the blood is followed by an increase in the amount of urea in the liver and urine, and of glycogen in the liver.

According to Seegen, the liver contains at the instant when life ceases 0·4 to 0·6 per cent. of sugar (Bernard, 0·2 to 0·3 per cent.; Dalton, 0·2 to 0·4 per cent.; Pavy, 0·02 to 0·05 per cent.)

Also while carotid blood and mixed venous blood from the right side of the heart contain about the same amount of sugar (0·109 to 0·153 per cent., a little in excess of the portal blood,) the blood of the hepatic vein contains *twice as much sugar as the portal vein* (SEEGEN).

Bernard thought that the glycogen of the liver, formed from the starchy matter of food, is stored up and converted gradually into sugar by a ferment in the liver.

This ferment Bernard believed he had isolated, but it has since been shown that any soluble albuminous body may be made to yield a solution capable of converting starch into sugar (LÉPINE), such sugar being always a glucose, while the sugar produced by true ferments (*e.g.*, ptyalin, diastase) has a slighter reducing action with a greater rotatory power and is probably identical with *maltose*. According to Dastre, the liver contains no diastatic ferment, but the liver cells possess the power of converting sucrose into glucose.

Again, according to Bernard, as the sugar is formed the glycogen should diminish; there should be a definite relation between them; this, Bernard thought he had proved.

Seegen thought he had disproved this in the following manner: Having first ascertained that glycogen is always evenly distributed throughout the liver, and is not accumulated in certain parts of it, he took a piece of the liver of a recently-killed or of a still-living animal, weighed it, scalded it, and determined the glycogen and sugar it contained. This operation was repeated at intervals with other portions of the liver. In this manner he discovered that the amount of sugar increases steadily from the moment of death, a process which appears to correspond with the death of the liver tissue and the cessation of its metabolic activity. On the other hand the glycogen does not undergo any corresponding diminution, except in rabbits in which it begins to dwindle at once and diminishes rapidly as the production of sugar increases.

Seegen denied that glycogen is the source of sugar, and suggests that the liver converts peptone into sugar. He found that when peptone solutions were introduced into the stomachs of dogs the liver sugar was increased by from 50 to 200 per cent.

He also observed that when peptone solution was injected into the portal, vein in 30—40 minutes the liver sugar increased from 100 to 300 per cent.

He also estimated the amount of sugar which passes into the hepatic vein of a dog, and has found that the amount of carbon in the food of a dog on meat diet, neither losing nor gaining weight, is sufficient to account for the carbon of the sugar.

He therefore held that sugar formation is a normal function of the liver, the quantity being considerable, 1000 grammes in twenty-four hours for a man weighing 80 kilos, the sugar being decomposed in the body.

He believed that this is a true liver sugar distinct from that derived from glycogen, that it is formed in the liver *post mortem*, but not at the expense of the glycogen present, that it does not disappear if the animal is starved or fed entirely on fatty food, and that it is formed from peptone, for after feeding with peptone its quantity becomes increased three-fold.

It seems to be admitted on all hands that carbo-hydrates may be formed in the body from proteids, either by splitting off (PAVY), or by complete decomposition and building up again (PFLÜGER), and it is even contended by some that every 100 grammes of albumen converted into urea yields 45 grammes of sugar, or for every gramme of nitrogen eliminated

by the urine 2·8 grammes of sugar are formed. It is believed that this formation of sugar takes place in the liver. Obviously when we reflect on its various sources the amount of sugar produced in the liver must be enormous, yet what becomes of it? Pavy maintains that there is less sugar in the hepatic vein than in the portal vein, and although he is in this respect stoutly opposed by Seegen, who in sixty-four observations found the sugar increased from 80 to 100 per cent. in the hepatic vein, he has found many observers to support his assertion that arterial blood contains no more sugar than venous blood (ABELES, BECK and HOFFMANN). Chauveau and Kaufmann find that arterial *always* contains more sugar than venous blood, so that it may be wise for the present not to abandon the notion that sugar is poured into the circulation by the liver in such quantities as can be dealt with by the tissues, in which it is ultimately utilised and decomposed.

But it has been asked, What becomes of the enormously larger amount of glycogen formed by vegetable feeding animals? The slow and sedentary ox does not seem likely to use up as much glucose as the restless tiger, and Pavy thinks this difficulty so great as to be fatal to the above explanation. But modern physiologists admit that carbohydrates may be stored in the body, not only as glycogen but as fat, and that it is in the latter form that the excess of sugar accumulates in the bodies of vegetable feeding animals.

EXPERIMENTAL GLYCOSURIA.

Glycosuria may be produced experimentally on animals by various lesions.

Since Claude Bernard discovered that sugar appeared in the urine of an animal after puncture of the floor of the fourth ventricle, an immense mass of facts of a similar order has been accumulated, so that now it would seem as if almost any lesion of the nervous system, central or peripheral, may cause glycosuria, while a whole host of toxic substances have been shown to possess, with more or less certainty, the same power.

In addition to the "Diabetic Puncture," the following lesions of the nervous system are stated to be followed by glycosuria:—

1.—Injury to the *vermiform process* of the *cerebellum* (ECKHARD).

2.—Section of the *Spinal Cord* at various levels (SCHIFF).

3.—Section of the *anterior cervical nerve roots* causes permanent glycosuria; section of corresponding *posterior roots* causes only temporary glycosuria (SCHIFF); artificial neuritis of the *first pair of dorsal nerves* (ARTHAUD and BUTTE).

4.—Destruction of various *sympathetic ganglia, e.g.*, the superior and inferior cervical (PAVY); the first thoracic (ECKHARD); the abdominal (KLEBS).

5.—Section of the splanchnic nerves (HENSEN), or ligaturing them (ARTHAUD and BUTTE).

Glycosuria caused by puncture of the floor of the fourth ventricle may be set aside by section of the splanchnic nerves. Other experimenters too have found that section of the splanchnics is not followed by glycosuria, and Cyon explains this by supposing the operation to give rise to such general dilatation of the intestinal blood-vessels that there is not enough blood to increase the circulation through the liver. He says, if the hepatic vessels be first dilated and the spinal cord and splanchnics then cut, the formation of sugar is not arrested.

6.—Glycosuria in certain cases follows irritation of the *right vagus* nerve (ARTHAUD and BUTTE).

7.—Similar results may follow section and stimulation of the central end of an ordinary sensori-motor nerve, such as the sciatic (SCHIFF).

8.—According to von Mering and Minkowski the complete removal of the *pancreas* in dogs is always followed by glycosuria, but this is prevented by leaving a small part of the gland even though the duct be removed. The result therefore cannot be due to the absence of pancreatic juice in the intestine. Lépine suggests that the pancreas forms a sugar-destroying ferment which is absorbed by the veins and carried to the liver by the portal vein. He performed the following experiment: Two dogs were chosen of equal size and kept fasting for 36 hours, the pancreas was then completely removed from one, and both were left unfed for 60 hours, when they were bled to death. In the blood from the one without the pancreas there was nearly three times as large a percentage of sugar as in the blood of the other, while in fifteen hours the blood of the latter had lost 33 per cent. of its sugar, while that of the former dog had lost only 6 per cent.

Minkowski has given the results of further experiments on this point. It is noteworthy that dogs deprived of the pancreas, present not only glycosuria, but all the charac-

teristic symptoms of diabetes, polyuria, thirst, hunger, and emaciation; the glycogen rapidly disappears from the liver, and there is diminished absorption of albumens and fats. After partial extirpation of the pancreas as a rule diabetes mellitus does not appear, even when the remaining portion is no longer connected with the intestine. Still, these remaining portions must not be too small. In two cases in which the remaining pieces of the pancreas had only $\frac{1}{15}$th or $\frac{1}{25}$th the size of the normal organ glycosuria in its severest form was observed similar to that after total extirpation. It is doubtful in these cases whether the remaining portions retain their functions.

In two other cases after partial extirpation a transitory glycosuria occurred, which only continued a few hours, and later even after abundant carbo-hydrate food it did not return; this transitory glycosuria may perhaps be regarded as a result of the injury which the rest of the pancreas had suffered by the operation.

In one case, by partial extirpation of the pancreas, diabetes was produced corresponding to the slight form of this disease in man. In a dog weighing 12 kilos, a portion of the pancreas, 31 grammes in weight, was removed; only the outermost point of the tail end remaining. No sugar appeared in the urine for the next five days, even when the dog was fed with meat and milk. But after carbo-hydrates sugar appeared in the urine. After 20 grammes of grape sugar, 78 appeared in the urine. By flesh diet the sugar disappeared from the urine, to return again in great amount after a diet of cane sugar. There was therefore, in this case, after the partial extirpation of the pancreas, an injury of that specific function of this gland, the complete deficiency of which, after total extirpation, causes the severe form of glycosuria.

In a still more remarkable case, the pancreas was partially extirpated and the stump retaining its vascular attachments grafted below the skin of the abdomen. Even thus displaced the gland appeared capable of exercising its function, for the urine remained free from sugar; the graft was ultimately excised, and the dog became diabetic (MINKOWSKI and HÉDON).

Puncture of the floor of the fourth ventricle after extirpation of the pancreas, increases the glycosuria by 30 or 40 per cent. (HÉDON); while if the medulla be so divided that the liver is cut off from the sympathetic, no glycosuria follows extirpa-

tion of the pancreas (CHAUVEAU and KAUFMANN); on the other hand glycosuria follows puncture, but does not occur after removal of the pancreas in fasting animals (THIROLOIX).

Lépine also removed the pancreas from a starving dog, the operation being followed by glycosuria, which was temporarily controlled by injecting into the jugular vein chyle taken from the thoracic duct of another dog during digestion. He also found that chyle added to a solution of glucose, maintained at a temperature of 38° C, caused a sensible diminution of the amount of sugar in some hours. He also found that malt diastase diminished the glycosuria of an animal rendered diabetic by the removal of the pancreas. Chyle from an animal deprived of its pancreas had no effect upon sugar. Lannois, at the instigation of Lépine, made subcutaneous injections of pilocarpine on a diabetic woman with the result that there was a very notable diminution of the glycosuria, in consequence, it is suggested, of the stimulation of the pancreas by this drug.

Arthaud and Butte dispute the theory of Lépine on the ground of experiments in which they ligatured all the pancreatic veins of a dog, without increasing the amount of sugar.

On the other hand by ligaturing all the branches of the cœliac axis, except the hepatic artery, so as to cause an excessive flow of arterial blood to the liver, they caused glycosuria, and the animal died after three months. The pancreas showed no alteration, as its circulation had been re-established by the mesenteric artery which had not been tied.

Lépine now maintains that blood and chyle contain a powerful glycolytic ferment, which is absent or greatly diminished in animals deprived of the pancreas. He believes that this is a product of the internal secretion of the pancreas, and that normally it destroys a large part of the sugar before it reaches the liver. His statements lack confirmation, and the theory is a very unreasonable one, as it would imply a great waste of nutritive material. Kaufmann has suggested that the pancreas secretes a substance which exercises a controlling influence over the liver, and that in its absence this organ permits an excessive amount of sugar to pass into the circulation. Arthus denies the existence of Lépine's glycolytic ferment in living blood, and contends that it is a cadaveric phenomenon; and Hédon could find no glycolytic substance in the pancreas, nor any diabetogenic substance in diabetic blood.

9.—De Renzi and Reale say that glycosuria is caused by resection of the duodenum and extirpation of the salivary glands.

10.—Gley states that dogs deprived of their thyroids become temporarily glycosuric; but Minkowski denies this.

11.—Hay found that the injection of neutral salt solution into a ligatured loop of intestine was sometimes followed by glycosuria.

12.—Kolisch produced glycosuria by tying the superior mesenteric artery.

13.—Glycosuria may in addition be determined by procedures directly occasioning increased flow of blood to the liver, as in the following examples:—

a.—Tying the accessory branch of the portal vein in frogs, so as to make the whole of the abdominal blood pass through the liver (SCHIFF).

b.—Irritation of the liver with needles (SCHIFF) or by electricity (PAVY).

c.—Compression of the aorta or portal vein.

d.—Injecting defibrinated arterialised blood into the portal vein.

The same phenomena may also be caused by a great many toxic substances:—

a.—By the inhalation of chloroform, of carbonic acid, carbonic oxide, sulphuretted hydrogen and carbon disulphide.

b.—By strychnine (M. FOSTER), salicylic acid (BURTON), phosphoric acid (PAVY), turpentine (ALMÉN), corrosive sublimate (ROSENBACH), uranium nitrate (LECONTE), benzol, acetone, aldehyde, ether, chloral, amyl nitrite, amyl alcohol, morphia, opium, and curare.*

c.—Dimethyl æthal carbinol (THIERFELDER).

d—Phloridzin.

Phloridzin is a glucoside discovered in 1885, by von Kormick, in the bark of apple, pear, cherry and plum trees. It forms silky, shining, needle-like crystals, soluble in cold water. Its formula is—

$$C_{21}H_{24}O_{10} + H_2O$$

which may break up into—

$C_{15}H_{14}O_5$ and $C_6H_{12}O_6$
Phloretin. Phlorosin.

* Ashdown believed that in many cases it is glycuronic acid and not glucose which appears in the urine in these circumstances (*op. cit.*).

The latter substance has the formula of sugar, and like it reduces copper salts and undergoes fermentation. When phloridzin is administered to animals it causes glycosuria, even when the liver has been rendered free from glycogen, or extirpated. The action of this substance has been studied by von Mering, who considers that he has proved that the substance excreted is really grape sugar, and not phlorosin.

Phloridzin caused glycosuria when given by the mouth or injected subcutaneously, or introduced into the veins. The sugar in the blood was not increased, while the hepatic glycogen diminished. The glycosuria continued even when the animal was starved for a long period. Occasionally in long-standing cases acetone and β-oxybutyric acid were present in the urine, and symptoms like diabetic coma occurred. The sugar was shown to be derived from the albumens of the body.

Phloretin is the only decomposition product of phloridzin which produced glycosuria; phlorose, phloritinic acid and phloroglucin being inert.

After the administration of phloridzin and chloral-hydrate, sugar and uro-chloral acid appeared in the urine.

Phloridzin was given to three persons, and sugar in considerable quantity formed in their urines. One gramme of phloridzin caused a daily excretion of 97 grammes of sugar; on the day after the phloridzin was stopped the sugar disappeared. No ill effects were produced through the use of the drug, which was continued for a month.

Zuntz proved that when injected into one renal artery, it caused glycosuria from the corresponding kidney only, for at least half-an-hour, and Minkowski found that after extirpation of the kidneys the administration of phloridzin was not followed by any increase of sugar in the blood; in man also the ingestion of phloridzin causes glycosuria without hyperglycæmia. Where the renal epithelium is already gravely compromised, phloridzin may fail to cause glycosuria, as was the case in seven out of ten cases of granular kidney to whom Klemperer administered it.

As phloridzin causes no increase of sugar in the blood, von Noorden believes it causes glycosuria by paralysing the renal epithelium so as to permit the passage of sugar into the urine.

With reference to some of these effects it is of interest to note that Masoni states that curare diabetes may be prevented by the previous administration of arsenic, while Kirk thinks

that the substances found in the urine of persons taking salicylates are chiefly other reducing bodies but that a trace of sugar may perhaps be produced by the action of the salt on the blood corpuscles.

It has been already mentioned that ligature of the bile ducts causes glycogen to disappear from the liver, and under these circumstances puncture of the floor of the fourth ventricle fails to cause glycosuria (WICKHAM LEGG, VON WITTICH, E. KÜLZ, FRERICHS). Wyatt has recently related the case of an old diabetic lady in whom the sugar disappeared from the urine during an attack of jaundice, but this, though usual, does not always follow, as the following case shows :—

CASE 28.—*Diabetes Mellitus—early diarrhœa—intercurrent jaundice—persistence of glycosuria.*

William J., aged forty-five, blacksmith, attended as an out-patient on June 12th, 1887, complaining of pain in the loins and hypochondrium. His illness began twelve months before with diarrhœa, and three months later this was followed with jaundice, which had persisted. His urine was dark amber, acid, 1026, loaded with sugar, containing a faint haze of albumen and a little bile pigment.

PATHOGENY OF DIABETES.

The true bearing of all these facts upon the pathogenesis of diabetes must remain for the present unsettled.

Let us take note for a moment of the gaps in our knowledge.

1.—It is not known definitely in what form the products of saccharine and starchy food leave the liver, whether as sugar in small quantities to be rapidly destroyed, or partly as sugar and partly as fat, as Pavy thinks.

2.—It is not known by what paths the influence of the various nerve lesions, which produce glycosuria, reaches the liver, though this is probably through the pneumogastrics (ARTHAUD and BUTTE).

3.—We are still uncertain of the nature of the influence of the pancreas on the production of sugar.

Until these questions have been settled we have not a proper basis for a rational pathology of diabetes.

There are two main theories which receive a large amount of support : 1, that of overproduction by the liver : 2, that of diminished destruction by the tissues ; and to these we may add, 3, paralysis of the renal epithelium, which is a return to the old view of the renal origin of diabetes.

The first of these is generally accepted, and modern opinion

inclines to the view that the overproduction is the consequence of either direct nerve stimulus to the hepatic cells, or removal of some influence which normally controls them, *e.g.*, the pancreatic secretion. Pavy, as is well known, regards the excessive activity, or as he thinks it, morbid function of the liver, to be due to vaso-motor paralysis; but Michael Foster points out that strychnine poisoning, in which the vessels are strongly contracted, causes glycosuria. It is possible that strychnine causes a rapid discharge of sugar before the vaso-motor spasm has taken place; but the curious effects of phloridzin indicate that in the action of drugs we may have to do with a quite different mechanism.

Hamilton, accepting the vaso-motor theory, says there are two possible modes in which it may act: (1) By diminishing glycogenesis, so that the sugar brought to the liver leaves it unchanged; and in support of this he quotes Ehrlich's observation that very little or no glycogen can be found in fragments of liver withdrawn by a trochar from diabetics during life; (2) By excessive conversion of glycogen into sugar.

Kaufmann, in support of the theory that diabetes is the result of overproduction of sugar by the liver cells, has shown that suppression of the function of the liver diminishes the amount of sugar in the blood of dogs rendered artificially diabetic as well as in that of healthy animals. He points to the observations of Voit and Leo which show that diabetics use up as much oxygen and excrete as much CO_2 as healthy persons, and his analyses of venous and arterial blood indicate that the tissues consume the same amount of sugar in diabetic and healthy animals.

The view that glycosuria depends upon non-destruction or diminished consumption of sugar in the tissues has been maintained by Seegen and Ebstein, and has recently found a brilliant defender in von Noorden.

Von Noorden explains that in health the carbo-hydrates are stored up in the body as glycogen and fat, while a certain proportion is constantly consumed by the tissues. If a greater quantity reaches the tissues than these can consume, the surplus appears in the urine. Glycosuria following Bernard's puncture, results from this injury causing the liver to suddenly discharge its store of glycogen, giving rise to hyperglycæmia and temporary glycosuria. An analogous result is seen in the glycosuria which follows concussion and apoplexy, while the

glycosuria which sometimes follows attacks of biliary colic is comparable to the discharge of glycogen which follows ligature of the bile duct, but these can only cause temporary glycosuria. In diabetes there is no proof of over-production of sugar, the occurrence of which could only be admitted when the excretion of sugar exceeds the sugar derived from the food, including that formed from albumens as well as that due to carbo-hydrates. He confesses that the observations of Kaufmann, already quoted, as well as those of Leo and Voit, are opposed to his views, but he doubts the accuracy of the methods in use for the estimation of sugar in the blood. Yet he has to make the important admission that the natural glycogen reservoirs (liver, muscle, etc.) must have become insufficient, and that the body must also have lost its capacity to compress sugar molecules into fat. That the influence of the nervous system upon the liver is limited to causing a discharge of glycogen is disproved by the fact that puncture will cause glycosuria in an animal which has been starved for a week and which therefore no longer has glycogen stored up in its liver (THIROLOIX). But it seems to me that the admission, that the liver has lost its power to retain glycogen, and passes into the circulation in the form of sugar all the carbo-hydrates it receives, concedes nearly all the other side claims. The only point is whether the production of sugar is an active vital function of the liver cells or the result of some defective power; in either case, an excessive output of sugar is the consequence.

I think the balance of evidence in favour of those who believe in the theory of over-production by the liver as the cause of diabetes, and I incline to the opinion that this is an excess of a normal vital function of the liver cells.

The third theory need not detain us; it merely amounts to a suggestion that glycosuria may under certain circumstances be of a renal origin. Klemperer believes that this condition exists, but is extremely rare. We not very uncommonly meet with cases in which slight glycosuria accompanies well-marked albuminuria and other signs of chronic Bright's disease in elderly persons, and these may be examples of this renal glycosuria. Jacoby, of Strasburg, has observed glycosuria in rabbits fed on carrots, when diuresis was produced by caffeine, and glycosuria has been observed to accompany the diuresis caused by digitalis. Klemperer has observed a case of interstitial nephritis with slight glycosuria, which was not

increased by a diet composed largely of carbo-hydrates, or diminished by exclusive meat diet.

I shall only mention the theory of Cantani and B. W. Foster, that the liver in diabetes forms an inoxidisable form of sugar, the so-called para-glucose, as this is not supported by any recent observations.

Apart altogether from this hepatic pathology are the theories of Ziemssen and Latham, who place the production of sugar in the muscles. According to Latham a degeneration takes place in the muscle albumen due to vaso-motor paralysis and vascular dilatation, leading to imperfect oxidation and the production of sugar in the following manner: the lowest cyan-alcohol $CH_2\begin{cases}OH\\OH\end{cases}$ instead of being oxidised to CO_2 and H_2O, is stopped at $CH_2\begin{cases}OH\\COOH,\end{cases}$ glycollic acid; this by further oxidation forms methyl aldehyde, thus :—

$$CH_2\begin{cases}OH\\COOH\end{cases} + O = CO_2 + \begin{cases}H\\COH\end{cases} + H_2O$$

Then six molecules of methyl aldehyde may condense, as has been shown to occur in plants, to form glucose thus :—

$$6HCOH = C_6H_{12}O_6$$

But if this were true the venous blood in diabetes should show an excess of sugar, which is certainly not the case.

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CHAPTER XVII.

ETIOLOGY OF DIABETES

PREDISPOSING CAUSES.

Geographical Distribution.—Very little has been hitherto published respecting the geographical distribution of diabetes. This is in part due to the absence of trustworthy statistical data and also because the incidence of a disease, the mortality of which is on an average less than 1 per 50,000 of population, is a subject upon which the experience of individual practitioners must be a fallacious guide. By the kindness of numerous friends I have been able to obtain statistics from which the following figures are calculated (1891).

TABLE I.

Showing the mortality from Diabetes Mellitus in some of the principal cities of Europe.

Name.	Rate per 100,000 of population.	Name.	Rate per 100,000 of population.
Paris *	9·6	Dresden	4·6
Copenhagen † ...	7·2	Vienna	4·2
Leipzig	6·4	Christiania	3·9
London	5·88	Naples	3·2
Berlin	5·04	Rome	1·67

* Paris has since risen to 14, as shown in Table II.
† This includes 72 provincial towns also.

These figures are calculated from the averages of five years at least, and are probably fairly trustworthy, as the registration in these cities is carefully carried out.

Trousseau regarded the disease as rare in Paris, and there can be no doubt that it has greatly increased of late years, as shown in the following table compiled by Dr. Jacques Bertillon, Chef des travaux statistiques de la ville de Paris.

TABLE II.

Mortality from Diabetes Mellitus in Paris for each 100,000 of population.

1865-69	1870-71	1872-75	1876-80	1881-85	1886	1887	1888	1889	1890	1891	1892	1893
4	3	3	5	8	11	12	13	14	13	13	12	14

English statistics show no such rapid rise of late years either in London or the country: in both the rate per 100,000 of population was, in 1893, only a little over 7.

TABLE III.

Showing the mortality from Diabetes Mellitus in certain European countries and British colonies (1891).

Name.	Rate per 100,000 of population.	Name.	Rate per 100,000 of population.
England	5·8	Western Australia	1·9
Ireland	3·2	New Zealand	2·6
Scotland	2·1	Jamaica	1·7
Prussia	1·3	British Guiana ...	0·24
Norway	1·9	Montserrat	6·0
Italy	1·6	Bahamas	0·2
Gibraltar	6·8	St. Kitts	0·2
Malta	13·1	Bermuda	0·7
Cyprus	no deaths	Natal	0·7
Heligoland	„ „	St. Helena	0·5
New South Wales	2·7	Sierra Leone	0·16
Victoria	1·6	Ceylon *	2·4
Queensland	0·8	Hongkong	0·1
Tasmania	3·2	Mauritius	1·4
South Australia ...	1·6		

* Said to be untrustworthy.

The figures for the Colonies are based on official statistics supplied me through the Colonial Office by the courtesy of the Rt. Hon. Lord Knutsford, at that time Secretary of State for the Colonies, and are calculated on the average of ten years. In addition to those placed in the table the following were returned as having had no deaths from diabetes registered within the period taken (the last ten years); viz., Fiji, Trinidad, St. Lucia, St. Vincent, Nevis, Antigua, Dominica, Virgin Islands, Falkland Islands, Lagos and Labuan. There was no general return from Barbadoes, but the mortality is

estimated at 1 per 100,000 of population; Cape Town has an estimated mortality of only 0·4 per 100,000; and there is no return from the Gold Coast, but the principal medical officer reports the disease to be very rare.

With respect to Ceylon, the principal colonial medical officer, Dr. W. R. Kinsey, writes in his official despatch to the Secretary of State: "The Registrar-General's figures, if forwarded without explanation, will convey a very erroneous idea of the prevalence of diabetes in Ceylon, because the registration of causes of death is wholly unreliable, as no medical certificate is required . . . . and the natives of Ceylon are peculiarly sensitive on the subject of diabetes; they consider it disgraceful to have it, they never speak of it, and conceal its existence as long as they can, for it is looked upon as a punishment for illgotten wealth, and that it is necessarily fatal and unamenable to treatment." He goes on to say that "it is most prevalent amongst the well-to-do natives." One doctor in private practice informed him that he sees in his practice an average of two fresh cases of diabetes a week, and that temporary glycosuria is very frequent. He has no hesitation in saying that it is a common disease among all races, alike among Hindus (Tamils), Mahommedans, and Cingalese. It is certainly hereditary and most common among the well-to-do class. He is thoroughly of opinion that over-indulgence in starchy foods and sugar, combined with sedentary habits and resulting corpulence, and sexual excesses, indeed, excesses of any kind, are important factors in its causation; he thinks that congestions of the liver which are apt to occur in hot climates in those persons who indulge freely in the pleasures of the table, favour its production. He believes it to be much more common in males than in females, and between the ages of thirty-five and fifty, while it is very rare in children.

It has not been possible to obtain any official statistics respecting the mortality or incidence of diabetes in India, but there is strong testimony to its occurrence very commonly in all parts of that country. In answer to my enquiries, Surgeon-General Cornish (late of the Madras presidency) wrote to me as follows:—

"The frequency of diabetes amongst the better classes, *i.e.*, those who do not engage in manual labour, is a matter of common notoriety amongst Indian practitioners. The causes of the disease I am not so clear about. Diet, chiefly farin-

aceous, oily, and saccharine, may have something to do with it. But personal habits in regard to venery and other things may also have to be considered. It should be noted also that young India is subject to much brain stimulation.

"The craving for higher education and for learning western ideas through a foreign language may unduly stimulate the mental and reasoning faculties in bodies perhaps insufficiently nourished and undeveloped. Whatever the causes are, we practically find some of the best intellects in India prematurely extinguished by diabetes.

"Over and over again it has been within my experience to find that the most promising men amongst the lawyers and university graduates have been cut off in the prime of life by this disease.

"Since I left India, I think the subject has attracted attention in Calcutta, and I daresay the *Indian Medical Gazette*, of the last five years, may give you some facts in regard to the matter. My own observations seemed to show that the educated and learned classes (chiefly non-flesh eaters) suffered in the greatest proportion, and that it was rare to find men of these classes lasting to a robust old age. The subject is a very interesting one, and well merits searching inquiry."

Norman Chevers wrote to the same effect, referring to its frequency among rich elderly natives in Calcutta, many of whom are fat and indolent, and immoderately fond of sweetmeats. The editor of the *Indian Medical Gazette*, writing in 1871, stated that among the upper and middle classes of natives in Calcutta almost every family had lost one or more of its members from this disease.

No statistical information could be obtained from the Straits Settlements (Singapore), but the disease is said to be not uncommon. A statement was forwarded from a Chinese doctor, in which he observed that while the disease is very rare in China, in Singapore he had met with seven or eight cases, in fifteen years' practice. Dr. Graham, of Sumatra, wrote that in seven years' practice among 15,000 Chinese labourers, he had met with only one case.

The statement of the Chinese doctor above quoted, concerning the rarity of diabetes in China, has been fully borne out by all the information I have been able to obtain. Dr. Burge, of Shanghai, was exceedingly kind in making enquiries amongst his colleagues, and their unanimous testimony is that

the disease is very rare in China. It is also equally rare in Japan, so far as my information extends.

The statistics from Mauritius were followed by a report of a discussion on Diabetes, which was instituted in the local medical society as a result of Lord Knutsford's circular, and this fully bore out the testimony of the figures that the disease is rare in the island. The fact, taken together with the rarity of the disease in British Guiana, is interesting, because both countries employ a large number of natives of India as coolies on sugar plantations. It seems to afford a strong confirmation of the views expressed by Indian practitioners in favour of the exemption of those classes engaged in manual labour. From Madagascar no statistics were obtainable, but Mr. S. Blackwell Fenn stated that it is very rare.

No statistics were to be obtained from Persia, but Dr. Tholozan kindly wrote me a letter giving me the result of his long experience in that country. He believes it is less frequent than in Europe, and more common in individuals of Turkish race than among native Persians. He attributes the disease to the immoderate use of rice, sweet sherbets and sweetmeats.

Dr. Hessenauer wrote that in five years' practice he had not met with a single case of the disease in Palestine. The official statistics of the town of Smyrna were applied for but did not come to hand, though they were promised. My application to official sources for statistics for Egypt was refused on the ground of insufficient clerical assistance to compile the information, but Dr. Grant Bey kindly wrote me that the disease is not uncommon and that according to his experience it prevails chiefly among Europeans, Syrians and Turks, the Copts and Arabs being less subject to the disease, though not exempt.

In Cyprus there had been no death from diabetes for ten years, and the chief medical officer in ten years' practice had seen only two cases, one in a Cypriot.

Respecting America, it was found very difficult to get any information of value. Tyson estimates the mortality from diabetes in Philadelphia at 11 per 10,000 deaths, and in New York 7, whereas in London the proportion is 26, and in all England 25.

According to the editor of the *New York Medical Record* the mortality from diabetes in the United States was 837 or 2·1 per 100,000 living in 1870, and 1443 or 2·8 per 100,000

living in 1880. The article goes on to say that glycosuria is very prevalent in the north-west where the air is very dry, business competition exceedingly keen and nervous wear and tear consequently very great. It is to be feared that at present no statistics can be obtained in the United States which can be fairly compared with the figures obtained from European sources. The disease seems to be rare in California, the statistics of San Francisco returning the mortality at only 0·6 per 100,000 living. Dr. Gresham, of Los Angeles, wrote that in seven years' practice he had not met with a single case. From South America it is even more difficult to get any information. Dr. Louis Colbourne, of Buenos Ayres, wrote that there are no statistics, but that in his opinion it is very rare, and Dr. Harvey reported the same of Chili. Its rarity in British Guiana is shown by the figure in Table III., and this is confirmed by a private letter from Mr. C. Macnamara, lately Colonial Surgeon at Essequibo.

This information, by no means complete, has been obtained with a vast amount of labour, and probably represents all or nearly all that can be learnt upon the subject at present.

These figures show that the African and Mongolian races enjoy considerable immunity from the disease in their own countries. Dr. Tyson, of Philadelphia, (U.S.A.) has stated that he has never seen a case in a negro in the United States, but he has informed me since making this statement that he has been assured of the existence of such cases.

The high rate of mortality in Malta is very remarkable, and it is curious that the report was not accompanied by any comment by the officer who sent in the figures.

There might at first sight appear to be a decided advantage in the country over the towns, as the great cities have a far higher average than the countries in which they are situated; but it must be remembered that the country statistics are always less reliable than the towns, and if we look to English figures we find reason to think that there is no such immunity in country districts. Taking the average of England and Wales as 25 per 10,000 deaths, we find the following counties above the average :—

Berkshire	100	Lincolnshire	70
Cambridgeshire ...	90	Buckinghamshire . .	64
Oxfordshire	80	Suffolk	60
*Rutland	80	Sussex	

*The figures are too small to be of value.

These are not counties in which many large towns exist. On the other hand the following counties, teeming with urban populations, give the following figures:—

Yorkshire...	31	Lancashire	22
Staffordshire	30	Warwickshire	17

In Scotland and Ireland the same facts are apparent, though in these countries the figures to be dealt with are so small that there is too much risk of fallacy for us to lay much stress upon them.

It is stated that in France diabetes is very common in the province of Normandy. Dr. Coldstream, of Florence, who kindly obtained for me a good deal of information respecting what is known of the incidence of the disease in Italy, points out that it is more prevalent in Tuscany than in the rest of that kingdom.

Race.—Diabetes mellitus is not confined to the human race. It is said to occur spontaneously among dogs (FERRARO), and to be more common among those kept for sporting purposes (ROBERTSON). Its frequency among Jews is well known; Frerichs has stated that out of his 400 cases, 102 belonged to this race of people. It does not appear, however, that other semitic nations suffer in the same way, unless we accept Dr. Tholozan's opinion concerning the special liability of the Turks as indicating this. Scudamore thought the Scottish people were specially liable to diabetes, and Fagge made use of this supposed liability as an argument against the relation of diabetes to gout, but there is no statistical evidence in its favour. Prout believed that red hair was particularly common among diabetic subjects, and Fagge endorsed this opinion, but the fact itself is doubtful, and its relation to race still more so. The apparent immunity of the Mongolian and African races has been referred to in the preceding section.

Prevalence of Diabetes.—In the ten years from 1884 to 1893, 17,794 persons were registered as dying of diabetes mellitus in England and Wales. This is a very great rise over the number given by Roberts as dying in the decade 1851–60, which was only 4,546, and there can be no doubt that the disease is increasing in this country (see Table IV., next page), the proportion to the total mortality having risen in these fifteen years (1878–1893) nearly 90 per cent., and to the population more than 70 per cent.

TABLE IV.

Year.	Deaths from Diabetes.	Total Deaths.	Proportion per 10,000 Deaths.	Proportion per 100,000 Living.
1878	1057	539,872	19	4·2
1879	1048	526,255	20	4·1
1880	1059	528,524	20	4·1
1881	1237	491,935	25	4·7
1882	1253	516,654	24·4	4·7
1883	1369	522,997	26	5·1
1884	1475	530,828	27·6	5·4
1885	1522	522,750	29	5·5
1886	1634	537,276	30	5·9
1887	1750	530,758	32	6·18
1888	1773	511,071	34	8·19
1889	1754	518,353	33	6·00
1890	1863	562,248	33	6·40
1891	1930	587,925	32	6·60
1892	2011	569,684	35	7·30
1893	2082	569,958	36	7·20

Age.—Diabetes occurs at all ages, but is less common at the two extremes of life. The youngest instance known to me is a case recorded by Deane in an infant aged three weeks.

Schmitz gives the following table of the ages of his 600 patients.

TABLE V.

1 to 10.	10 to 20.	20 to 30.	30 to 40.	40 to 50.	50 to 60.	60 to 70.	70 to 80.
5	25	56	104	134	196	60	20

Pavy has tabulated his 1500 cases under the age at which the disease sets in.

TABLE VI.

Age.	Actual Number.			Percentage Ratio.		
	Males.	Females.	Total.	Males.	Females.	Total.
Under 10	3	5	8	0·22	0·36	0·58
1 to 20	35	22	57	2·57	1·61	4·19
20 „ 30	69	28	97	5·07	2·05	7·13
30 „ 40	154	70	224	11·32	5·14	16·4
40 „ 50	260	79	339	19·11	5·80	24·92
50 „ 60	281	137	418	20·66	10·07	30·73
60 „ 70	138	44	182	10·14	3·23	13·37
70 „ 80	25	9	34	1·83	0·66	2·49
Over 80	1	—	1	0·07	—	0·07

The following table is taken from the Report of the Registrar-General for England for the year 1886.

TABLE VII.

All Ages.	Under 1	1	2	3	4	5	10	15	20	25	35	45	55	65	75	85 and upwards.
Males 978	2	2	5	1	—	8	22	40	43	110	118	143	246	189	49	—
Females 656	—	—	2	—	1	9	26	41	38	62	91	101	136	101	44	4
Total 1634	2	2	7	1	1	17	48	81	81	172	209	244	382	290	93	4

These tables all agree very closely, though the maximum mortality, as might be expected, occurs a few years later than the maximum of living cases. Thus Schmitz and Pavy agree in finding the largest number of cases between the ages of forty and sixty, while the maximum mortality is from fifty-five to seventy-five. This would appear to indicate that such elderly diabetics live a considerable time, which is strictly in accordance with our clinical knowledge.

Sex.—Diabetes is more common among men than women, in the proportion of rather more than 3 to 2. But this disparity does not seem to hold good amongst children. In Table VII. the numbers under twenty give 80 males to 79 females, the proportion under fifteen being 40 males to 38 females. In Table VI. (PAVY'S) there were 3 males to 5 females under ten years of age, though under twenty there were 38 males to 27 females; in Stern's 117 cases the girls were more numerous than the boys in the proportion of 5 to 3; as age advances the proportion becomes nearly 2 males to 1 female, until in old age it comes back to the equality of childhood.

Social Condition.—The reports from India and Ceylon emphasize the fact that the disease is most common among the well-to-do classes. This is also illustrated in a table compiled by Dr. Bertillon, showing the deaths from diabetes

in the various districts of Paris, distinguished according to the means of their inhabitants.

Arrondissements.	Deaths per 100,000 of Population.
Opera. R.*	20
Passy. R.	18
Elysée. V.R.	16
Temple. E.	16
Luxemburg. R.	15
Palais Bourbon. R.	14
Vaugirard. P.	14
Batignolles. E.	14
Hôtel-de-Ville. E.	13
St. Laurent. V.E.	12
Louvre. V.E.	11
Popincourt. P.	11
Neuilly. P.	11
Bourse. V.E.	10
Panthéon. E.	10
Gobelins. V.P.	9
Observatoire. P.	9
Montmartre. V.P.	9
Ménilmontant. V.P.	8
Buttes Chaumont. V.P.	7

*R. = Rich; V.R. = Very Rich; E. = Easy; V.E. = Very Easy; P. = Poor; V.P. = Very Poor.

Heredity. There can be no doubt that diabetes mellitus is hereditary. Chevers quotes the following statement from the *Indian Medical Gazette* for 1871: "In one of the most influential native families in Calcutta, No. 1 died of acute diabetes at the age of sixty-five; No. 2, his eldest son, died of chronic diabetes; No. 3, his third son, had chronic diabetes; No. 4, his fourth son, died of acute diabetes; No. 5, his daughter, aged sixty-five, had diabetes; No. 6, eldest son of No, 2, died of chronic diabetes; No. 7, second son of No. 2, had diabetes; No. 8, eldest son of No. 4, had diabetes." Thus the disease affected eight members of the same family, extending over three generations.

Auerbach has related the history of a family, in which the father died insane and the mother diabetic. Of eleven children, one died insane, one of diabetic coma, four others were insane, and one was diabetic. Frew has recorded a more remarkable case in a little girl aged nine, suffering from diabetes, whose paternal grandfather, uncle and aunt, had all died of the same disease.

Nevertheless in the majority of cases there is no evidence

that the disease has been inherited, and it is more common to obtain a history of a diabetic brother or sister than of a diabetic parent. This is perhaps due to obvious causes, as it is always exceedingly difficult to get information which goes back any number of years.

Trousseau thought that phthisical parents often had diabetic children, and there can be no doubt that a history of tubercular disease can often be traced in diabetics.

Excessive use of Sugar and Starchy Food.—There is a very widespread belief that the excessive use of sugar tends to diabetes. Eichhorst has met with the disease among the workpeople in sugar factories. Christie, who first described the prevalence of the disease in Ceylon, referred it to the excessive use of sugar and starchy food. Tholozan regards the disease among the Persians as caused by sweetmeats and sweet sherbets. Indian practitioners recognise the effects of the same causes; yet, as has already been mentioned, in Mauritius and British Guiana, where the people are chiefly employed in sugar factories, the disease is very rare. Charcot states that glycosuria is frequently produced among the novices in the Monastery of La Trappe. Collins has recorded two examples, one of which was persistent but disappeared under diet and opium.

Beer.—Kratschmer thinks that the urine of great beer drinkers always contains more or less sugar, but there is certainly no evidence that beer drinking *per se* is a common cause of diabetes. Were it so, it is scarcely conceivable that the kingdom of Prussia would occupy such a relatively favourable position in the table.

Cider has been said to have some relation to diabetes, and the prevalence of the disease in Normandy is ascribed to this cause, but the cider counties in England show a mortality much below the average.

Obesity.—Many diabetics are, or have been, very stout. It is generally in elderly persons that this connection is observed. Kisch has observed temporary glycosuria as a frequent occurrence in general obesity. Seegen said that 30 per cent. of the cases he had analysed were excessively fat at the beginning of their illness. Kisch says that in all cases where hereditary obesity comes on in youth and progresses rapidly, and in non-hereditary cases where treatment is not beneficial, diabetes must be looked for as a possible occurrence. He believes one-half of the former and 15 per cent. of the latter

become diabetic. In many families it can be shown that some members are fat from childhood and others are diabetic, or the fat individuals become diabetic about the fourth decade. It is probable that one of the first results of excess of sugar poured into the circulation is an increase of fat, and so long as the surplus sugar can be stored up in this way glycosuria is postponed. But a time comes when either the activity of the liver is greater and the sugar is more than can be so stored up, or the limits of the fat-forming capacity of the body are reached, and then sugar appears in the urine.

EXCITING CAUSES.

Frerichs gives the following classification of the causes of glycosuria.

1. *Toxic Glycosuria.*
   - Curare.
   - Carbonic oxide.
   - Amyl nitrite.
   - Ortho-nitro-phenyl-proprionic acid.
   - Methyl-delphinin.
   - Morphia.
   - Chloral.
   - Hydrocyanic acid.
   - Sulphuric acid.
   - Mercury.
   - Alcohol.

   Also from morbid poisons.
   - Cholera.
   - Anthrax.
   - Diphtheria.
   - Enteric fever.
   - Scarlatina.
   - Malaria.

2. *Glycosuria from Digestive disturbance.*
   - Gastric catarrh.
   - Gout.

3. *Glycosuria from Nervous disturbance.*
   - Psychoses.
   - Neuralgias.
   - Injuries to brain and cord.
   - Brain diseases. Apoplexies, aneurisms of cerebral arteries, meningitis cerebro-spinalis, etc.

But in many of these instances it is not certain that glycosuria occurs, and in most it is only transitory.

Chloroform.—This may not only give rise to temporary glycosuria, but occasionally causes acute and fatal diabetes (FORT).

Bromide of Potassium.—Weber has described a case of acute and fatal diabetes in a little girl of seven, the effect of swallowing an ounce of this drug, which she took by mistake.

Infective processes.—On the other hand, the morbid poisons or infective processes, as it is better to speak of them, are undoubtedly true causes of diabetes. Whether this effect is produced by the influence of their toxins on the nervous system, or whether they lower the vitality of the pancreas, and so permit it to be invaded by intestinal microbes which set up pancreatitis, may be uncertain. In this connection I may refer to the fact that Debove has collected fifty cases of diabetes, in five of which the husband and wife were attacked simultaneously. Lecorché, who had observed the same facts, attributed them to community of anxieties and nutriment; but Debove thinks that the lives of men and women are very different, and he remarks that husband and wife are rarely both gouty; though in England this is not uncommon, and possibly husbands and wives live a life more in common in England than in France. However, these observations on the frequent occurrence of diabetes in husband and wife are supported by Dreyfous, Gaucher, Labbé, Lettulle, Schmitz, and Rendu, and the inference is that under certain circumstances, or in some obscure way, diabetes may be contagious. Such a view is not altogether impossible, taking into account the number of infectious processes which exist, some of them little known to us, and many capable of running their course without marked derangement of health.

Acute Tonsillitis.—Rogers has published a case of acute tonsillitis in a gentleman aged forty-four, which was followed by diabetes, terminating fatally from coma twenty hours after being first recognised.

Diphtheria.—Glycosuria may follow diphtheria, as in a case reported by Zinn, which, however, ended in complete recovery after lasting ten weeks.

Erysipelas.—Glycosuria often occurs in connection with surgical sepsis, phlegmonous and gangrenous inflammations, anthrax, lymphangeitis and erysipelas, and true diabetes may follow.

CASE 29.—*Diabetes Mellitus—following erysipelas—loss of sexual desire—slight polyuria—slight thirst—no knee jerks—no wasting.*

Mr. Paul R., aged forty-eight, consulted me in March, 1888, complaining of diabetes, of which he had been aware for three or four months after an attack of erysipelas supervening in his foot from a cut got by treading on broken glass. The polyuria and thirst were slight, and there was no wasting; his chief complaint was his loss of sexual desire, which seemed to depress him mentally, although he was unmarried, His knee jerks were absent. The urine measured from four to five pints daily, sp. gr. 1029, loaded with sugar.

Influenza.—I have already published the notes of two cases of diabetes following attacks of influenza in the epidemic of 1889-90. They are of sufficient interest to be reproduced here:—

CASE 30.—The earlier in point of date was that of a girl named O.B., aged twenty-two; she had never been very strong, and at Christmas, 1889, she had an attack of influenza. Shortly after this she began to suffer from thirst and frequency of micturition, when she was passing about 100 oz. of urine daily containing 10 per cent. of sugar. The case improved under treatment but did not recover.

CASE 31.—C. A., a glassblower, aged thirty, was in bed for a week at the end of January, 1890, with a severe attack of Influenza. Immediately after this he began to suffer from thirst and loss of weight. He had been in the habit of weighing himself at intervals and was sure that up to the time of the attack of influenza he had not been getting thinner, but since then, though a spare man, he had lost 17 lbs. He was passing 200 to 300 ozs. of urine daily, containing 7 to 8 per cent. of sugar.

Malaria.—The importance of malaria as a cause of diabetes is doubtful. Burdel believes that glycosuria occurs very commonly in connection with this infection, and gives the following table of cases:—

	Cases.	Sugar.	Percentage.
Febris quotid. ...	134	29	22
„ tert. ...	122	17	14
„ quart. ...	76	11	14
„ perniciosa ...	11	3	27
Severe cachexia ...	40	32	80

Calmette supports this view, stating that while acute malarial affections are sometimes attended by transitory glycosuria, severe malarial cachexia is a distinct cause of diabetes.

On the other hand, in the course of a recent discussion at the Société Médicale, of Mauritius, the great majority of the speakers were opposed to the belief in any relation between these diseases, and this seems to be the general view of British practitioners residing in malarious countries. It is strange if this relationship were true that the disease should be so rare on

the West Coast of Africa and in British Guiana, while we should expect it to be more common in Italy than statistics show it to be. It is a point upon which additional information is wanted, and it is worth noting that the malarial counties of England are those which stand among the highest in the mortality from diabetes.

Enteric Fever.—The following case of diabetes followed enteric fever.

CASE 32.—*Diabetes Mellitus—following enteric fever—œdema of legs.*

Annie S. —, aged thirty-nine, housewife, was admitted to hospital on September 23rd, 1890, complaining of great thirst, increasing weakness, pain in eyes, and dimness of vision and polyuria. Duration thirteen months.

Family History.—Father and mother both dead, the former from apoplexy, aged forty-seven ; the later from cancer of liver, aged forty-nine.

Previous Health—Patient had measles when seven years old, scarlet fever when a baby, small-pox since marriage (at twenty-one), from which she quite recovered, and was in good health until thirteen months ago. In August, 1889, she had enteric fever for four months, and ever since she had suffered from thirst and polyuria.

Present Condition.—She was a fairly well developed woman, but ill nourished and thin ; there was no cyanosis or jaundice, but some slight œdema of legs ; skin moist. Temp. 98·4°. Resp. 16. Pulse 84.

Teeth good, gums red, tongue thick, marked at edges by the teeth and covered with a thick whitish fur ; appetite very good. Thirst very great ; had pains in the stomach when fasting ; bowels confined ; abdomen full, with some tenderness over the epigastrium ; there was no dulness on percussion.

Liver dulness in V.M.L., 4 inches.

Splenic dulness in M.A.L., 2 inches.

Respiration, 16. Movements of thorax, regular and equal. Percussion note resonant, V.R. and V.F. equal on both sides. Breath sounds normal ; no adventitious sounds were heard, but she had slight cough.

Heart sounds clear, no murmurs were heard ; cardiac dulness, upper limit, 3 C.C. Left limit internal to V.M.L. Right limit ¼ inch to right of sternum. Apex beat in 5th space internal to V.M.L.

Pulse 84, regular, full ; the tracing (*Fig.* 52) shows a very fair amount of tension. She had some dyspnœa on exertion, but not to any marked extent.

Fig. 52.

Urine quantity 76 oz. ; sp. gr. 1037 ; acid ; no albumen ; loaded with sugar ; complained of a burning sensation on passing water. Had always been regular until now, last time it was very scanty, and she had missed this time.

She was sensitive to pain, heat and cold ; no numbness or tingling, pupils equal, slightly dilated, responded readily to light. Patient could not see to read even with her glasses, but could see and distinguish in-

dividuals in a good light and could see much better with glasses; her sight was much worse the last six weeks. Hearing very good. Taste and smell unimpaired. Patellar reflexes were absent on both sides, both plantar reflexes present. Did not sleep well.

Syphilis.—From what has been said in connection with diseases of the nervous system, it will be readily understood that gummata in the brain may give rise to glycosuria or to all the symptoms of diabetes, but Ord believes he has met with several cases of glycosuria without any evidence that the medulla was implicated. Decker has reported a case of diabetes occurring in the course of a syphilitic affection of the eye, which was cured by mercurial inunction without any dietetic restrictions.

Soon after Christmas, 1889, I saw a man who had diabetes and a syphilitic sore mouth, but there were complicating factors in the etiology, as he had had influenza, and had received a severe blow on the loins from a heavy iron bar. Moreover anti-syphilitic treatment, which cured his mouth, did not cure the diabetes.

Decker attributed his case to syphilitic disease of the cerebral arteries.

Injuries.—Durham and Bellingham Smith state that glycosuria is an almost constant, although usually transitory, effect of injuries to the head and spine, but it generally passes off in four or five months, yet lasts sometimes as long as two years. They say that the later the onset the more grave the prognosis, and it is unquestionable that diabetes may be so engendered. In a case of Dale's, a child fell on the back of its head, and months later acute and fatal diabetes set in ; and in the case of an officer related by Moosdorf, he became diabetic after a bullet wound in the neck. Scheuplein has published the case of a young dragoon who fell from a window forty feet high, and dislocated the twelfth dorsal vertebra. He was treated by extension, but eleven days after the injury acute diabetes set in, which lasted about a month, and then gradually disappeared, the patient making a good recovery from his accident, and being quite well two years afterwards. Pavy has recorded a case following a kick from a horse. In a case of Ebstein's, a boy aged fourteen was struck by a stone in the region of the stomach. This was followed by pain and increase of the liver dulness, which gradually disappeared; but three months later diabetic symptoms set in. A patient of Lindsay's fell and struck his right loin. This was followed by pain and

local swelling, which disappeared in time, to be in turn followed by thirst, polyuria, and emaciation.

CASE 33.—*Diabetes Mellitus—due to a blow—thirst—polyuria—wasting.*

John B., fifty-four, wire drawer, admitted as an out-patient on March 12th, 1889, complaining of thirst and polyuria. He had been ill six months, and had been treated with brown bread *ad libitum* and codein (gr. j) three times a day. Just before this illness began he bruised his hip at his work. There was no family history of diabetes, but one of his grandfathers had gout. The quantity of water varied from 4½ to 6 pints, sp. gr. 1032-35, loaded with sugar. He weighed 7st. On probably the same diet, though he was told to eat bread very sparingly, Jambul perles (CHRISTY) given in as large a dose as four, three times a day, produced no effect: and as much could be said of antipyrin. The quantity of water gradually diminished to three or four pints, and his weight was 6 st. 13 lbs., on April 30th, 1889.

Redard has recorded a case in which a small abscess by the side of the rectum was accompanied by polyuria (2½ litres) and glycosuria, which symptoms disappeared when the abscess had completely healed. But in certain instances true diabetes may follow, as in a case recorded by Frerichs, where the exciting cause was an abscess connected with a tooth. Spencer says passing glycosuria is very frequent in association with carbuncles and severe boils, in patients whose urine was previously free from sugar. M'Nish has recorded the case of a blacksmith, aged fifty-six, who was severely burnt by a bottle of paraffin oil taking fire. Twelve days after the accident his urine became saccharine, and this continued for twenty-five days, until the burn was healed. Albert and de Renzi have observed glycosuria occurring in gangrene.

Malignant Disease.—Spencer has observed glycosuria in cases of malignant disease not affecting internal organs, but it does not amount to diabetes. In cancer of the pancreas true diabetes may develop; a very well-marked case of the kind was under the care of my colleague, Dr. Simon; and Dreschfeld has recorded one quite recently. The following case is an example of glycosuria in connection with malignant disease of the pancreas.

CASE 34.—*Diabetes mellitus—jaundice—cancer of pancreas.*

G. S., forty-four, labourer, was admitted with epigastric pain and jaundice, on June 22nd, 1895. He had been ill three months, and attributed drinking a great deal of beer and getting chilled when heated; the jaundice came on about a week later, and his motions were at first quite white. He had no pain for the first month, but since then it has been continuous, and aching in character, worse at night; it is localised and does not shoot in any direction, nor is it made worse by eating. Up to the time of this illness he

had always been a healthy man, and he comes of a family which has always been long-lived, though a brother, who was a hard drinker, died of an enlarged liver. On admission his conjunctiva and skin were stained deep yellow, and he complained of great irritation of the skin, for which he was always scratching himself. He was well developed and fairly well nourished, but had been losing weight; when weighed in the hospital, on July 7th, he was only 8 stone, and a fortnight later he had lost six pounds more. The right lobe of his thyroid was enlarged, but he attributed it to an injury received in an attempt to throttle him twenty years ago.

Temp. 97·6°. Pulse 72. Resp. 22.

He suffered from flatulence and pain after food, and his tongue was coated with a white fur, but there was no eructation or vomiting; his bowels were moved spontaneously. The abdomen was flat and retracted, somewhat tender every where, but allowing the enlarged liver to be felt projecting nearly a hand's breadth below the costal margin; it was quite smooth, and the gall bladder was distended. There was no ascites. The heart and lungs were normal. His urine was not increased in amount, but was a deep olive green colour; it gave all the tests for bile pigment, contained a trace of albumen, 364 grs. urea, 1240 grs. sugar, no casts. While in hospital on a diet from which sugar (but not carbohydrates) was excluded, he passed only two to three hundred grains of sugar, but, as already stated, he lost weight. I was away at the time, but he probably ate little, and we know that under such circumstances, digestion and absorption are both greatly diminished. He died some little time after this, and cancer of the head of the pancreas was found.

Cold.—Prout believed that cold acted as an exciting cause, and he quotes a case of Marsh's, where the patient had been exposed greatly to cold at sea for four days. Rollo quotes a case of Marshall's, which was apparently caused by drinking cold small beer when in a state of profuse perspiration; and Peiper relates the case of a girl, aged seventeen, who was attacked with symptoms of acute diabetes after drinking a glass of iced water when heated from dancing. She recovered after eight weeks' treatment. Poniklo has recorded a case in which at least temporary glycosuria followed eating iced cream.

Cold Climates certainly do not show any high mortality from diabetes, Scotland having a lower average mortality than Ireland, while Norway is still lower; Prussia has a lower mortality than Italy, and as we have seen the disease is very prevalent in India and Ceylon.

Lightning Stroke.—A case of diabetes following lightning stroke has been reported by Hermanides.

Nervous Diseases.—Maudsley and Savage consider diabetes in the parent is often followed by insanity in the child; on the other hand Schmitz states that 248 out of his 600 cases of diabetes had a family history of insanity.

Although glycosuria may occur in the course of many diseases of the central nervous system, especially in general paralysis of the insane (HAMILTON), and epilepsy (EBSTEIN), it is not very common. Bond met with it in 12 only out of 175 cases, and most of these showed an absence of many of the chief signs of diabetes. In two melancholics who recovered, the improvement in their mental condition coincided with the gradual disappearance of the glycosuria. The cases were:—

General paralysis . .	3
Melancholia ...	6
Organic Dementia ...	2
Senile Insanity ...	1

True diabetes is more often connected with some localised lesion, such as a tumour in the floor of the fourth ventricle or on the vagus nerve. It has been met with in association with locomotor ataxy of syphilitic origin (REUMONT), in insular sclerosis (EDWARDS, RICHARDIÈRE), and frequently after injuries to the head or spine. The association of diabetes with locomotor ataxy has been observed in the same family. In one case the mother was diabetic, in another the son, in a third the father, in a fourth the father and brother, and in a fifth the brother and nephew (GUNION and SOUQUES). My colleague, Dr. Stacey Wilson, has recorded a case of diabetes occurring in association with Friedreich's ataxy; death occurred from coma, and the brain, medulla and pancreas were stated to be normal. Shingleton Smith has recorded a case of glycosuria occurring in the later stages of a case of tumour of the cervical portion of the cord.

I have had under my care a curious case of acromegaly associated with enlarged thyroid and diabetes; she improved under treatment, but her mental condition was peculiar, and I lost sight of her after a time.

There is a considerable amount of evidence that mental emotion may often be the starting point of an attack of diabetes. Losses in business, family affliction, danger to life, etc., have been recorded as immediately preceding the onset of the disease.

The association between hysteria and diabetes has been insisted upon by Grenier, but without sufficient evidence that this amounts to anything more than a casual coincidence. It may be, however, that the diabetic dyscrasia, like plumbism, favours the development of hysteria.

Manby has recorded three interesting cases, illustrating the

connection between exophthalmic goitre and diabetes. In the first a diabetic father had two children, of whom one was diabetic and the other the subject of goitre, exophthalmos, and irregular action of the heart; in the second, one brother was diabetic, the other brother lost two children with acute diabetes, and the sister had Graves' disease; in the third, two sisters were diabetic, and a third the subject of Graves' disease. In connection with these observations it is interesting to note that transient glycosuria has been frequently observed during the administration of thyroid gland extract.

Acute Rheumatism.—Diabetes may follow acute rheumatism (HUGHES BENNETT), and Dyce Duckworth states that glycosuria is common in "chronic rheumatoid arthritis," which is, however, a somewhat ill-defined condition.

Gout.—Diabetes is a common phenomenon in gout; it is not uncommonly attended by polyuria and thirst, but there is very slight loss of weight.

CASE 35.—*Diabetes Mellitus—polyuria—thirst—albuminuria—gout—disappearance of sugar.*

Mr. Frederick W. W., aged fifty-six, consulted me first on March 31st 1883, being sent to me by my friend Mr. Eales, who had discovered sugar in his urine. He had been passing too much water for five months, and suffering from thirst. He had had gout several times. Weighed 13 st. 2 lbs.; had not lost flesh. Tongue clean; appetite good; bowels regular. Fundus of eyes normal. Urine, 1028, contained sugar and a trace of albumen. On anti-diabetic diet, using toast moderately, and extract of opium (gr. j) three times a day, his urine was diminished by two-thirds, its specific gravity came down to 1020, but there was some loss of flesh—by May 5th, he had lost 5lbs. By June 16th the sugar had disappeared, and did not return at all after June 30th. On his last visit, Aug. 18th, 1884, he weighed 13 st. 3 lbs., his urine amounted to two quarts daily; it was free from sugar and he felt very well.

Liver Diseases.—Roger asserts that he has met with glycosuria in various affections of the liver, including cirrhosis and persistent jaundice. Hull has recorded a case of severe and fatal diabetes which set in ten months after the bursting of an abscess of the gall bladder. Some years ago I attended with my friend, Dr. R. Norris, of Birchfields, a gentleman who had been suffering from diabetes, when he was suddenly attacked by jaundice, with complete obstruction of the common duct. The sugar disappeared from his urine and did not return after the bile regained its passage into the intestine.

Pregnancy.—Bennewitz, in 1828, recorded the case of a stout young woman, in whom diabetes with severe thirst

and polyuria came on during the fourth pregnancy, left her as soon as she was delivered, and recurred during the fifth and sixth pregnancies—leaving her during the intervals. Poulet has published the case of a girl of sixteen, who became pregnant at fifteen, and aborted at the eighth month. Soon after she began to suffer from thirst, polyuria and emaciation. Matthews Duncan, after reviewing the whole subject, formulated the following conclusions:—

1. Diabetes may come on during pregnancy.
2. Diabetes may occur only during pregnancy, being absent at other times.
3. It may cease with the termination of the pregnancy, returning sometime afterwards.
4. Diabetes may come on soon after parturition.
5. Diabetes may not return in a pregnancy occurring after its cure.
6. Pregnancy may occur in diabetes.
7. Pregnancy and parturition may apparently be unaffected in their healthy progress by diabetes.
8. Pregnancy is very liable to be interrupted in its course in diabetes, and probably always by the death of the fœtus.

There is no doubt that pregnancy may give rise to true diabetes, and that Griswold is wrong in asserting that it is always temporary glycosuria unworthy to be called diabetes, being attended by neither polyuria nor thirst nor any other symptom of diabetes.

Sinclair says that the glycosuria of lactation is always present in nursing women when the breasts become engorged with milk from weaning, death of the infant, or other cause, and he quotes numerous cases in support of his statement, but Davenport says that it is only when lactation has existed for five or six months that its sudden suspension gives rise to the presence in the urine of *lactose* in large quantities.

Climacteric Diabetes.—It was supposed by Lecorché that the climacteric period favoured the occurrence of diabetes in women. Unquestionably elderly women get diabetes, but in some instances, as in the following, there is an apparent connection between the two events.

CASE 36.—*Diabetes Mellitus—glycosuria—polyuria—wasting—sudden onset at the menopause—cystic goitre.*

Elizabeth K., fifty, attended as an out-patient on May 7th, 1889, complaining of thirst, hunger, and her "flesh all leaving her." She had been ill a year and nine months. She had never had gout, rheumatism, or any

serious illness or accident. She was married, and had had eight children. She knew of no member of her family who had suffered from diabetes or gout. Menstruation ceased quite suddenly at the time that these symptoms came on. Patient was a fairly developed woman, with a flushed face and dry skin; much emaciated, weighing only 7 stone. There were no symptoms of dyspepsia; her bowels were regular. She had a large cystic goitre, which she had had since puberty. Her pulse was quick, 144; physical signs normal. Urine, 1035, loaded with sugar. She had to rise three or four times each night to pass water.

Mr. Lawson Tait believes that it is of essentially good prognosis, and can be treated by opium alone without dietetic restrictions.

Imlach has recorded a remarkable case of a diabetic woman, aged thirty-one, on whom he operated for pyosalpinx by removal of the appendages, and in whom the operation was not only perfectly successful in curing the local trouble, but was followed by the complete disappearance of the diabetes.

Excessive sexual indulgence is apparently, at times, an exciting cause of diabetes. Dickinson mentions the case of a young man who died at the early age of twenty-five, in whom he could find no other cause but excessive promiscuous sexual indulgence, to which he had been addicted since the age of seventeen. *Masturbation* is another alleged cause, but Yarrow has recorded a case of temporary glycosuria attributed to enforced sexual *continence*. Under treatment with bromide of ammonium, fluid extract of jaborandi, and external local applications to the neck and loins, he recovered in eight days, and on the disappearance of the sugar a spontaneous pollution occurred!

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CHAPTER XVIII.

MORBID ANATOMY.

*(The Bradshaw Lecture delivered before the Royal College of Physicians in London, August 18th, 1890.)**

MR. PRESIDENT, FELLOWS OF THE ROYAL COLLEGE OF PHYSICIANS, AND GENTLEMEN :—It is my first duty to express my gratitude to you, and my humble acknowledgment of the honour done to me and I hope I may say to the city to which I belong, in selecting me to deliver the lecture which, by the pious munificence of his widow, annually commemorates the birthday of the late Dr. Bradshaw, a former Member of this College, and a worthy and esteemed physician, who practised during his lifetime in the town of Reading. It is fitting also that I should express on behalf of the College our respectful recognition of this lady's appreciation of the character and aims of our ancient corporation, by founding this lectureship for the promotion of the study of medicine. I feel deeply conscious of my own inability to perform the task so generously entrusted to me in such a manner as to deserve your praise ; but by your courtesy I know I may expect a patient hearing, and from your indulgence I trust I may escape your censure if I fail to attain the high level of excellence which has characterised the discourses of my eminent predecessors in this chair.

The subject I have chosen for your attention to-day is undoubtedly wanting in novelty, but I was induced to select it chiefly because it was a matter on which my thoughts were already engaged, and concerning which I possessed abundant materials for reinvestigation of the questions which have been raised in recent years, with the opportunity of studying them in the light of the most modern methods of histological research. If I have no new discoveries to announce, and if I must content myself rather with the humble position of a critic than that of a revealer of fresh facts or novel theories, I

* This lecture has been throughout revised and in part rewritten.

will at least ask you to believe that this has not been from any want of patient industry and careful thought, but because of the great difficulty of making new observations in a field which has engaged the close attention of so many competent observers.

It is my purpose to lay before you an account of the changes observed in diabetes in the principal organs of the body and in the blood, concluding each description with comments upon points of interest on which my own observations seem to me to have thrown any light.

THE NERVOUS SYSTEM.

Brain.—Though no constant lesion has been observed in the brain, this organ is seldom normal. This statement is at variance with the statistics of cases accumulated from all sources (WINDLE), but is in harmony with recent observations. Out of twenty-seven cases of which I have records of necropsies, the brain was stated to be normal in only five. The most common description given is that it was "œdematous and congested, with thickened membranes," eleven out of the twenty-two abnormal brains presenting more or less of these characteristics. It is less often described as anæmic. Atrophy of the convolutions has been stated to be common (MACKENZIE); but this does not accord with my observations. These changes are, of course, not peculiar to diabetes, and cannot be considered to have any special relation to its pathology. In quite a minority of cases localised lesions are found, the value of which differs greatly, and in many instances is not easily appraised. Among the most important are tumours in the fourth ventricle and medulla, of which a relatively small number only have been recorded. Not a single instance has come under my own observation, and I have only found records of ten cases, of which three were published by Frerichs. Of the direct dependence of the diabetes upon the growth in many of these cases there can be no reasonable doubt. Instances have also been recorded of softening (LUYS); of the presence of corpora amylacea and colloid masses (ABRAHAM); of localised alterations in colour and congestion (TARDIEU); and of enlargement of the peri-vascular spaces (DICKINSON). Of these the softening alone is of undoubted value. The congestion and dark colour of the medulla are interesting, but, taken by themselves, prove little; while the enlargement of the peri-vascular spaces is too

common in non-diabetic brain disease, and too exceptional in diabetes, to count for much. The observations of Dr. Abraham are a valuable contribution to the histology of the diabetic brain, and possibly belong to the same class as other lesions, to which I shall refer immediately, which indicate failure of nutrition of the brain tissues, and are rather an effect than a cause of the disease.

There is undoubtedly a tendency in the diabetic brain to the formation of cysts in the white matter. I have found such cysts in the frontal lobes, in the medulla, and in the pons; while in another case a small focus of softening in each crus cerebri looked like an early stage in this process of cyst formation. These cysts are quite free from hæmatoidin staining. Some of them are so small as to be hardly worthy of the name of cysts, but others are as large as horsebeans. It seems probable that this condition is due to a failure of nutrition. The choroid plexuses also occasionally present abnormalities; thus I have found cysts on the choroid plexus of the left lateral ventricle, and the same structure in the fourth ventricle was in one case hypertrophied, while in another case the plexuses of the lateral ventricles were of a dark-purple colour, as if from congestion. The lateral ventricles and the *iter a tertio ad quartum ventriculum* have been found dilated without any mechanical obstruction to explain it. Thiroloix has recorded a case of diabetes in which the pancreas was normal, but a patch of sclerosis existed in the floor of the fourth ventricle. Extensive hæmorrhage into the brain substance is rare in diabetes. In Windle's tables there are only three examples in one hundred and eighty-four necropsies, or in 1·6 per cent. There has been no instance at the General Hospital for twenty years out of a total number of one hundred and twenty cases with twenty-nine deaths. Dickinson has, however, described minute hæmorrhages as common. Finally, glycogen has been found in large quantities in the medulla oblongata and in the vessels of the cerebral cortex (FUTTERER). Zaleski found iron present, but we are still in doubt as to how far this is an abnormality.

On careful microscopical examination I have not been able to detect, even with the most modern technical methods, any constant histological changes either in the cortex, the basal ganglia, or the medulla. The latter has been the subject of special investigation, but the only positive fact observed has been that the capillaries of the vagus nucleus in one case

seemed to be abnormally numerous and full of blood. The specimen has been placed under one of the microscopes. I have looked for minute hæmorrhages without finding them, and the absence of blood pigment in the cysts already alluded to is opposed to the view that these originate in that fashion. While not disputing its occasional occurrence, hæmorrhage is certainly not a constant or common form of lesion in the diabetic brain.

Spinal Cord.—In a certain number of cases diabetes has followed the extension of diseased processes from the spinal cord into the medulla, as in locomotor ataxy and insular sclerosis, where the disease is unquestionably the result of the lesion of the medulla. Sandmeyer has published a case of diabetes in which a small patch of degeneration was found in Goll's columns occupying the anterior half at the cervical enlargement and the anterior two-thirds in the upper cervical region. The pancreas was normal. Williamson has found in two cases pallor of the posterior columns very visible after hardening in Müller's fluid, and escaping the action of staining agents, but under the microscope very slight atrophic changes could be seen. I have been unable to confirm these observations in the cords which have come under my notice. Again, diabetes has not infrequently followed injuries to the spinal column, though in one case where this occurred the cord was apparently uninjured. In connexion with these facts, it will be remembered that Schiff has produced artificial glycosuria by dividing the cord opposite the second dorsal vertebra; but in cases where the diabetes is neither a complication of a recognised disease of the cord nor a consequence of injury to the spine, this structure has been usually described as normal. Unfortunately, the number of cases in which it has been carefully examined is not large, but in these enough has been found to show that secondary nutritive changes, similar to those in the brain, are apt to occur in the cord; these are dilatation of the central canal, enlargement of the peri-vascular sheaths, and localised softening. Tumours of the cord in connection with diabetes have been very rarely recorded; the only case known to me is one of myxoma of the dura mater (SHINGLETON SMITH). Glycogen has been found in large quantities in the spinal cord. Microscopical examination of the spinal cord, stained after Weigert's method, has been carefully carried out without any special change being noted.

Cerebro-spinal Nerves.—Tumours situated on or compressing the vagus nerve have been found associated with diabetes. Three such cases have been recorded (HARLEY, HENROT, FRERICHS), and in each instance the right nerve was the seat of the lesion. In Frerichs' case the tumour encroached upon the floor of the fourth ventricle, but in the other two cases no such complication existed, the tumour being situated in the thorax. These observations are very interesting in connection with the recent experiments of Arthaud and Butte, who found that artificially induced neuritis of the central end of the divided vagus caused glycosuria, while a similar lesion of the peripheral end caused hunger, wasting, polyuria, and thirst. Lubimoff has found in one case of diabetes atrophy and pigmentation of the inferior ganglion of the vagus. Few pathological observations on the spinal nerves in diabetes are known to me, but it is noteworthy that Arthaud and Butte

Fig. 58. Right Median Nerve showing very advanced interstitial and parenchymatous neuritis. Osmic acid preparation.

have produced glycosuria by setting up neuritis in the roots of the first dorsal pair of spinal nerves. Schiff, moreover, has shown that stimulation of the central end of any sensori-motor

nerve, such as the sciatic, may be followed by glycosuria. Clinical observation has revealed the existence of a secondary diabetic neuritis, which may be multiple (LEYDEN), or attack particular nerves (ALTHAUS). In these circumstances it gives rise to the phenomena of paralysis, with wasting and loss of faradaic response of the muscles supplied by the affected nerves. In other instances we may meet with a general peripheral neuritis closely resembling locomotor ataxy in its clinical features, and, as we shall see, very hard to distinguish from it. There is a widespread interstitial and segmentary neuritis with great increase of the connective tissue. In the cord some swelling and pigmentation of nerve cells only has been observed. The accompanying drawing (*Fig.* 53) is from a case under my care which will be described further on.

Sympathetic Nerves.—Changes in this system of nerves in diabetes seem very early to have attracted the attention of pathologists. Thus Duncan, as long ago as 1818, found the sympathetic in the abdomen three times as thick as normal; and Percy, in 1842, described the semilunar ganglia, the splanchnic nerves and vagus, as thickened and of cartilaginous hardness. Klebs and Ph. Munk, in 1870, found changes in the cœliac plexus with destruction of a number of ganglion cells, and Cavazzani has observed atrophy, pigmentation and necrosis of nerve cells with increase of the connective tissue, nuclei and fibres. Lubimoff has also found sclerosis of the sympathetic ganglia and atrophy of their nerve cells. In four of my cases the semilunar ganglia have been found enlarged, in two cases atrophied, with increase of connective tissue and atrophy of nerve cells, and in one, embedded in a dense mass of fibrous tissue. Hale White has recently described similar lesions in four cases of diabetes. On the other hand Shingleton Smith has made numerous observations on the state of the sympathetic ganglia without finding any uniform or definite change. In three of my cases the semi lunar ganglia were normal, and I have shown in a paper published in the *British Medical Journal* in 1883 that similar microscopical changes to those above described are met with apart from diabetes. Yet I have never seen the semilunar ganglia enlarged except in diabetes; in some of my cases the right semilunar ganglion was quite twice the normal size. The importance of these facts depends upon the results of experiments which have shown that destruction of various sympathetic ganglia—for example, the superior and inferior

cervical (PAVY), the first thoracic (ECKHARD), and the abdominal (KLEBS),—and division or ligature of the splanchnic nerves (HENSEN, ARTHAUD and BUTTE), are followed by glycosuria. Extirpation of the cœliac plexus is followed by wasting and death, with temporary glycosuria and acetonuria (LUSTIG, PEIPER).

THE CIRCULATORY SYSTEM.

Heart.—In about 40 per cent. of my cases the heart has been described as free from noticeable change; while in about the same proportion it has been described as pale and soft;

Fig. 84. Heart muscle from a case of very advanced fatty and fibroid degeneration. Fat droplets stained black with osmic acid. (Hartnack oc. 2, obj. 7. Tube drawn out.)

more rarely, dilated or hypertrophied, or distinctly fatty. Pericarditis occurs occasionally, and, in one case of death from a carbuncle in a diabetic subject, the pericardium was full of fluid, fatty blood. Valvular disease is quite exceptional, though Lecorché has described endocarditis as a complication of diabetes, and Maguire has recorded a case. It is said to occur in the later stages, and to affect usually the auricular surface of the mitral valve. The rarity of endocarditis may be estimated from the occurrence of only one

case of valvular disease out of the ninety-four cases collected in Windle's tables; and in my twenty-nine cases there was valvular thickening in one only. Mayer has stated that out of three hundred and eighty diabetics seen at Carlsbad, eighty-two, or 24 per cent., showed signs of cardiac enlargement, and Schmitz, of Neuenahr, has made a still stronger statement as to the prevalence of fatty heart. Frerichs has drawn attention to glycogenic degeneration of the cardiac muscle, and suggests that this is the real cause of the cardiac debility of diabetes. Hypertrophy of the heart was present in 13 per cent. of cases examined in the Berlin Pathological Institute, and this accords very nearly with my experience. Fatty heart is probably much more common, if we are to judge by the frequency with which the muscular substance is described as pale and soft in reports of diabetic necropsies; yet I should estimate it as occurring in less than 40 per cent. of all cases. The preceding illustration (*Fig.* 54) shows the appearance of the muscle in a very marked case. Glycogenic deposits in the

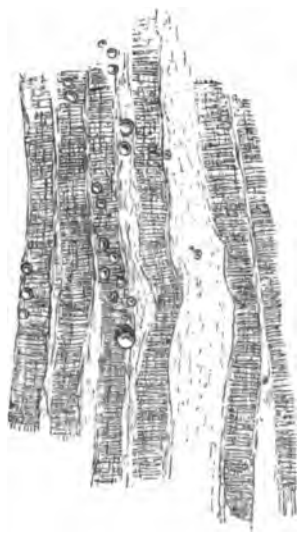

Fig. 55. Heart muscle apparently healthy, except for a few granules of glycogen lying within the sheaths of the muscular bundles. (Hartnack, oc. 2, obj. 7. Tube drawn out.)

wall of the heart have only been found by me in such small quantity that I cannot ascribe to them any serious pathological significance. The drawing (*Fig.* 55) shows a few granules of

glycogen deposited between the muscular bundles, but the muscular fibre appears healthy.

Blood.—The blood of diabetics generally looks normal to the naked eye. It is sometimes described as dark, and is sometimes very obviously loaded with fat, a white, cream-like layer rising to the surface when the blood is allowed to stand. Under the microscope the fat is seen to be at first in a state of molecular subdivision, but these molecules run together to form droplets after death, and this may produce the appearance of capillary embolisms. Occasionally the red blood-corpuscles are found broken down into a granular material (FOSTER, VON JAKSCH). In one of my cases the leucocytes were peculiarly large. Quantitative changes in the hæmocytes are common, these being generally reduced in number, with a corresponding reduction in the hæmoglobin. Normal blood contains sugar in varying amounts. The following table gives the estimate of four observers :—

Name.	Parts per cent.
Pavy	0·078 to 0·081 (dog).
Otto	0·10 „ 0·14 „
Seegen	0·15 „ 0·19 (man).
Frerichs	0·12 „ 0·3 „

According to Seegen, the amount present in mild cases of diabetes does not exceed the normal, but in severe cases it may rise as high as 0·4 parts per cent. The alkalinity of the blood serum is reduced, owing to the presence of certain organic acids of doubtful identity, of which diacetic acid and β-oxybutyric acid seem the most probable. The existence of acetone is disputed, as former reports of its presence are believed to be due to the breaking up of diacetic acid to form acetone and carbonic acid gas. In certain experiments conducted by me some years ago in the laboratory of Professor Tilden, at Mason College, I was unable to detect any acetone in the blood of a diabetic patient who had died of coma.

THE RESPIRATORY SYSTEM.

Lungs.—Pathological alterations in the lungs are the rule in diabetics, and perhaps no organ shows more constant changes. In my cases 17 per cent. only were free from disease. The

most common condition was congestion, or congestion and œdema. The next most frequent alteration was phthisis, which was present in 27 per cent. Small foci of softening were observed in one case, abscess in one, hæmorrhagic infarcts in one, and gangrene also in one. Dreschfeld has described the following types of lung affection in diabetes: (1) Acute croupous pneumonia, very acute and fatal, but rare; (2) acute broncho-pneumonia, which may terminate by gangrene; (3) chronic caseating tubercular broncho-pneumonia, the common form of diabetic lung complication; (4) chronic non-tubercular broncho-pneumonia; (5) gangrene of the lung. Fink recognises two forms of diabetic phthisis: (1) Tubercular and (2) fibroid. In the latter there are no tubercle bacilli in the sputa of lung, no caseous deposits, and the lung undergoes chronic induration. Non-tubercular phthisis is not so common as used to be imagined; at least I have almost invariably been able to find tubercle bacilli in the sputa, but an undoubted example, with most careful *post mortem* examination has been placed on record by Roque Devic and Huguenenq. Pleurisy and empyema occur rarely. Fat embolisms have been described as playing an important part in the pathology of diabetic coma (SANDERS and HAMILTON), but it is doubtful if they are not *post mortem* formations, due to the running together of the fat which was previously held suspended in a molecular state, and in any case they are not present in such numbers as to give rise to any symptoms (SAUNDBY and BARLING). The vessels of the lungs have been described as undergoing hyaline and fibroid thickening; but this is not a primary change, or one in any way peculiar to diabetes.

THE DIGESTIVE SYSTEM.

Liver.—Great interest attaches to this organ, because of its physiological relations to sugar formation. An opinion was at one time held, and has been expressed by recognised authorities, that the liver in diabetes is usually healthy, and even a more than usually healthy appearance has been described as characteristic of it. In my experience this is a very erroneous view. The liver is generally enlarged, weighing from sixty to eighty ounces. In a smaller number it is small, pale, and soft. Fatty degeneration is very common; congestion is often observed; the consistence of the organ is sometimes abnormally firm. A certain degree of interstitial hepatitis is

frequently present, and occasionally this goes so far as to produce distinct cirrhosis. This is attributed by Letulle to the effect of the abnormal destruction of hæmocytes. Hanot and Schachman have also described this form of cirrhosis. The liver is sometimes smooth, at others granular and scarred. The lesion begins, according to these observers, around the radicals of the hepatic vein, but Brault and Gaillard point out, in my opinion rightly, that the new growth begins in both the hepatic and portal areas. A form of cirrhosis is associated with bronzing of the skin (diabète bronzé). Some degree of interstitial hepatitis may, however, be seen without any evidence of pigmentary deposit in the liver or the integument (*Fig.* 56). This drawing shows very well marked commencing

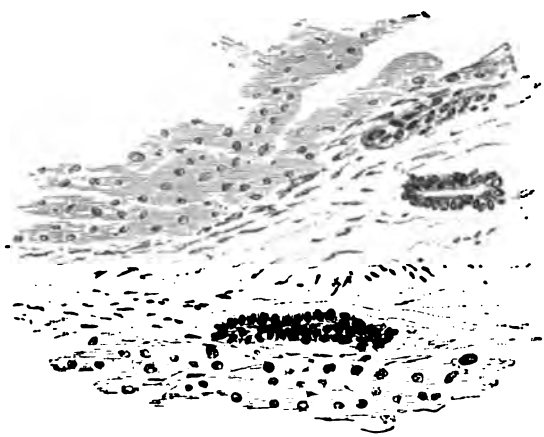

Fig. 56. Section of liver showing commencing interstitial hepatitis in a portal canal. Two newly formed biliary canaliculi are seen near the edges of the acini. (Hartnack, oc. 3, obj. 7. Tube drawn out.)

cirrhosis in a diabetic liver, Abscess of the liver is sometimes met with associated with diabetes. I remember one such case when I was a pathologist, and I believe it presented all the clinical phenomena of severe diabetes. The liver contained one large abscess and numerous smaller ones. A similar case was reported in the U.S. Navy Reports for 1878. It is permissible to believe that the abscess in these instances was really the cause of the diabetes. Dickinson has described thrombosis of the branches of the portal vein, and angeiomata formed of dilated capillaries near the radicals of the hepatic vein. In spite of its fatty appearance Weyl and Apt have not

found the diabetic liver to contain an excessive amount of fat:—

Normal liver - - - -	3·70 pts. per mille.
Diabetic liver - - - -	3·75 „ „

Moreover, absence of fat from the liver cells has been observed by Beale and Frerichs. Quincke described excess of iron in the liver, deposited in the form of granules. Zaleski has not observed it in granular form; he estimates the diabetic liver to contain 0·685 parts of iron per mille, but he points out that we have no data to enable this to be compared with the normal quantity.

Spleen.—This organ is very frequently described as normal, but the most common naked-eye change is that it is small, pale and soft. It is more rarely enlarged and congested, and sometimes contains tubercle. It is said to contain excess of iron (QUINCKE), but, as already explained, data are wanting as to the amount present in health. Glycogen has also been found in it. Hyaline degeneration of the small arteries has been described, but I have not been able to perceive anything abnormal about them.

Pancreas.—Dr. Baumel, in a paper published in the *Montpellier Médical* for 1881-82 was the first to contend that disease of the pancreas was the regular cause of diabetes, and in the same communication he recorded a case of diabetes without emaciation (*diabète gras*) in which this association existed. To him, therefore, belongs by right any honour that is due to the writer who first distinctly recognised the full significance of the pancreatic lesion in diabetes. But it was Lancereaux who drew general attention to the frequency with which the pancreas is atrophied in diabetes, and he went so far as to associate the clinical type of *diabète maigre* with this lesion. The importance of these pathological observations first became manifest when the experiments of Minkowski, Lépine, and others showed that extirpation of the pancreas in animals is followed by diabetes. This organ is by no means so carefully examined by pathologists as it deserves to be, and there is wanting that familiarity with its ordinary naked-eye and microscopic appearances which gives value to their descriptions. In many cases no note of its condition has been made. The following table shows the state of the

pancreas in twenty-seven cases examined in the General Hospital:—

Pancreas	atrophied and fibrous	-	11
„	„ „ soft	-	2
„	enlarged „ „	-	1
„	„ „ hard	-	3
„	„	-	3
„	congested (mottled)	-	1
„	normal	-	6

so that it was normal in only 23 per cent. So far as my own observations go, I am disposed to agree with Lancereaux, as I have found the pancreas shrunken in all my cases of typical wasting diabetes, but Lépine has seen atrophy of the pancreas in a fat diabetic subject. That the pancreas stands in some relation to diabetes is shown by the experience of Bull, of New York, whose patient died of diabetes after he had extirpated the pancreas. Duffey and Dreschfeld have published cases of diabetes associated with cancer of the pancreas; and a very well marked example of the same kind was under my care last summer. Churton has recorded a case of pancreatic cyst associated with diabetes. In a review article (August 2nd, 1890) the editor of the *Philadelphia Medical News* referred to a case of cystic disease of the pancreas from a case of diabetes exhibited by Longstreth in 1877, and to one of multiple pancreatic abscesses with glycosuria reported by Frison in 1875; on the other hand, he stated that Langenhans had recently published a case of necrosis of the pancreas in which there was no sugar in the urine. Numerous collections of cases of pancreatic diabetes have been since published by Vaughan Harley, Williamson, J. G. Hoppe-Seyler, Hansemann, Fleiner and others. In the cases of pancreatic disease collected by Dr. Handfield Jones, and more recently by another distinguished Fellow of this College, Dr. Norman Moore, there is no mention of diabetes. It has been suggested, (1) that the pancreas supplies the liver with the fatty acids necessary to the formation of bile acids from glycogen, hence, in affections of the pancreas there is excess of glycogen with resulting diabetes (POPPER); (2) excessive production of glucose from diastatic ferments formed in the stomach and duodenum (BOUCHARDAT); (3) the formation of paraglucose by the action of modified pancreatic juice (CANTANI); (4) the absorption of the pancreatic ferment, which, passing direct to the liver, changes the glycogen to glucose

(BAUMEL); (5) the suppression of a normal sugar-destroying ferment which should pass by the pancreatic lymphatics to mingle with the chyle (LÉPINE); and (6) that the pancreas regulates in some manner the sugar-producing function of the liver (KAUFMANN). Brault and Gaillard have described a pigmentary cirrhosis of the pancreas analogous to the pigmentary cirrhosis of the liver observed in diabetes. Pancreatic calculi may cause cystic degeneration or sclerosis, or complete adipose transformation.

The drawing (*Fig.* 57) is a low-power view of a portion of

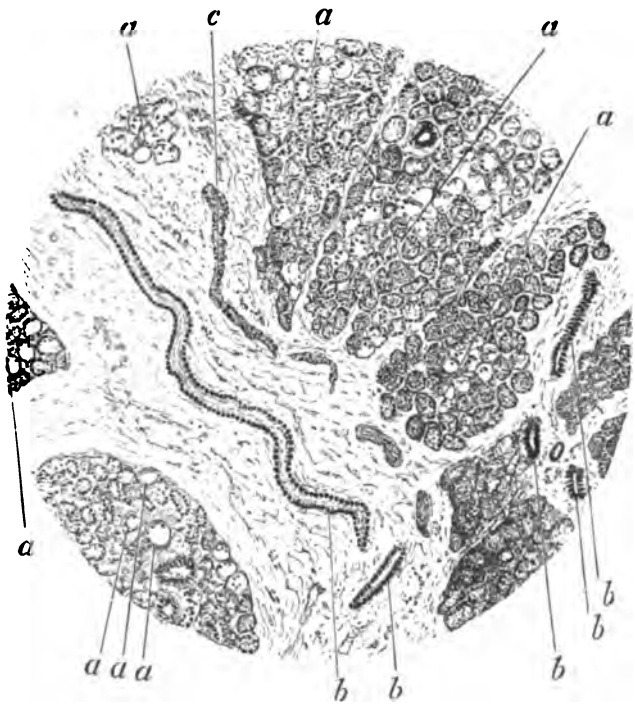

Fig. 57. Section of atrophic cirrhotic pancreas, showing great increase of connective tissue with *a*, hyaline degeneration of glandular epithelium; *b*, newly formed ducts, and *c*, ducts undergoing atrophy. (Hartnack, oc. 2, obj. 4. Tube drawn out.)

pancreas, showing great increase of connective tissue with a new formation (?) of ducts and a hyaline condition of parts of the pancreatic glandular epithelium. The latter appearance shown in *Fig.* 58, which was formerly thought to be a morbid change, is probably only a physiological condition of the cells

distended with secretion. It is evident that there is an increase of fibrous tissue with destruction of the gland analogous to

Fig. 58.—Highly magnified view of a group of pancreatic acini which have undergone hyaline transformation. (Hartnack, oc. 8, obj. 7. Tube drawn out.)

cirrhosis of the liver. This process is undoubtedly inflammation and not simple atrophy. In the earlier stages of the process the gland is swollen from abundant infiltration of its tissue with round cells. A section of such a swollen pancreas, obtained from a case of rather acute diabetes, is shown under one of the microscopes (*Fig.* 59).

It has been suggested that the atrophy of the pancreas may be secondary to disease of the cœliac plexus; but Lustig found that extirpation of this plexus was not followed by atrophy of the pancreas; and this has been confirmed by Peiper.

Stomach.—It is unfortunate that the stomach is often omitted in *post mortem* reports. I have notes of its condition in only eleven cases, but it is significant that in only one instance was it found to present no morbid alteration. In three cases it was dilated, in three there were hæmorrhages generally near the pyloric end, in two the mucous lining was congested, in one softened, and in one in a state of chronic catarrh. Windle speaks of "thickening" of the mucous membrane as not uncommon, and also of distension of the organ by gas.

Intestines.—The large bowel is generally found filled with hardened fæcal masses, and congestion or catarrhal conditions of the mucous membrane are not uncommon. Hæmorrhages

similar to those in the stomach also occur in the duodenum. In two instances large masses of tænia medio-canellata were present. The mesenteric glands were twice found to be enlarged. Frerichs has described a dysenteric condition of

Fig. 60.—Section of enlarged pancreas showing commencing cirrhosis with infiltration of the connective tissue spaces by round cells. (Hartnack, oc. 2, obj. 4. Tube drawn out.)

the large intestine, and Ebstein desquamation of the epithelium lining the bowel.

GENITO-URINARY SYSTEM.

Kidneys.—In not one of my cases were the kidneys described as normal, though in many the changes were not of great importance. The most common condition appears to be a slight degree of fatty degeneration. This comes out in Windle's tables as well as my own. Such kidneys are generally enlarged, and their capsules are often adherent. Less commonly the kidneys are enlarged and congested. Sometimes there is thinning of the cortex, or distinct contraction of the organ. Tubercle and lardaceous disease occur occasionally, and the kidney may become gangrenous (TURNER). The above-mentioned fatty change has been described specially by

Fichtner, who regards it as characteristic of diabetes. But the most interesting histological fact in the diabetic kidney is the hyaline degeneration of the tubular epithelium, which was first described by Armanni. His observations were confirmed by Ebstein, who assigned the seat of the lesion to the descending limb of Henle's tubes; but this was disputed by Ferraro, who, however, found the change nowhere outside the medullary portion of the kidney. This last observer attributed the changes to a primary lesion of the vascular walls. These changes in the epithelium and the co-existing hyaline changes in the vessels were well described by a distinguished Fellow of this College, Dr. Stephen Mackenzie, in opening a discussion at the Pathological Society of London in 1883. Ehrlich also described, "as characteristic of and peculiar to diabetes," a hyaline degeneration of the epithelium of that part of the kidney between the cortex and the pyramid—that is, the boundary zone; and Strauss proved that this lesion is identical with that described by Armanni. Strauss found that it was only present in one out of three cases, but he agreed that it is absolutely characteristic of diabetes, and he attributed it to the osmosis of sugar into the cells. Ehrlich considered that the change was due to glycogenic infiltration of the cells, but Strauss, in a later paper, says that no glycogen may be visible, even when all Ehrlich's precautions are taken. With reference to its causation, Albertoni and Pisenti have investigated the changes produced by administering small doses of acetone to rabbits. They found the following lesions: (1) granular degeneration of the epithelium of the convoluted tubes, the nuclei still staining well; (2) complete destruction of the epithelium with disappearance of the nuclei, and slight dilatation of Bowman's capsules; the glomeruli and connective tissue were not affected. They suggest the possibility that the necrosis of the epithelium observed by Ebstein may be due to the action of acetone on the kidneys. Stokvis, too, found that artificial diabetes, produced by injecting grape sugar into the blood, caused albuminuria; and he believes that this sets up a chronic nephritis. Both these are possible explanations of the fatty change already alluded to, which is entirely like that of slight chronic parenchymatous nephritis due to infective disease; but they do not throw any light upon this peculiar and characteristic hyaline change. My observations entirely confirm the existence of this hyaline degeneration and its restriction to the epithelium of Henle's tubes. It is

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well shown in the illustration (*Fig.* 60), and is quite different

Fig. 60.—Portion of Henle's looped tube, showing hyaline degeneration of the epithelium Armanni's lesion. (Hartnack, oc. 2, obj. 7. Tube drawn out.)

Fig. 61.—Renal tubule showing masses of glycogen within the epithelial cells or free. (Hartnack, oc. 2, obj. 7. Tube drawn out.)

from the glycogenic infiltration which may also be present, as shown in the drawing (*Fig.* 61), though this fails to bring

out the characteristic mahogany staining of the glycogen granules. The kidneys, like many other organs in diabetes, may present marked fatty degeneration (*Fig.* 62), droplets

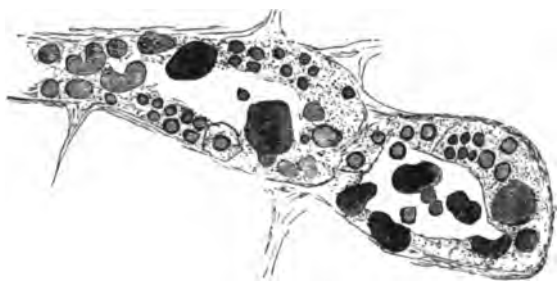

Fig. 62.—Portion of renal tubule showing fat droplets, stained black with osmic acid, lying within the epithelial cells or free in the lumen. (Hartnack, oc. 3, obj. 7. Tube drawn out.)

staining black with osmic acid being abundantly visible within the epithelial cells and free in the lumina of the tubules, the straight tubules being chiefly affected. Not uncommonly the kidneys present all the characteristic features of chronic diffuse nephritis, as is illustrated by one of the microscopic specimens.

Bladder.—This organ is usually normal, but it is often dilated and hypertrophied. The mucous lining sometimes may be the seat of hæmorrhages.

Ovaries.—Israel has described a case in which there was gangrene of both ovaries associated with recent general peritonitis. These organs have also been described as cystic and atrophied, but these are common conditions, and not in any way specially associated with diabetes.

Concluding remarks.—It is very plain that diabetes, far from having no morbid anatomy, has one of a very complicated kind, and one that cannot be without bearing upon its pathology. Definite changes in the medulla and vagi are undoubtedly causative, but are exceedingly rare. The most important common lesion is the wasting of the pancreas; of some significance, too, are the alterations in the abdominal sympathetic ganglia, though they are too inconstant to form the basis of a satisfactory theory. The liver changes are probably altogether secondary to a functional hyperæmia induced under nervous influence. The appearances in kidneys, lungs, heart, and brain are mainly the results of defective nutrition and of long-standing hyperglycæmia.

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CHAPTER XIX.

CLINICAL HISTORY.

SYMPTOMS.

DIABETES Mellitus presents itself for clinical observation under two types, (1) acute, (2) chronic, in which the essential symptoms, *wasting*, *thirst*, *polyuria* and *glycosuria* are present in varying degrees of intensity. In the former these are all great, in the latter the first three especially are moderate, and the total excretion, though perhaps not the actual percentage of sugar, is also not excessive. It does not appear to be practicable to refer the majority of cases of diabetes to their anatomical cause, but exceptionally we may recognise the dependence of the disease on some affection of the nervous system, pancreas, or liver.

In the acute type the patient is young, he looks ill, his face is pale or cyanosed, his expression is anxious, the hair rough, the skin dry, the lips parched, the tongue red and sticky or covered with a black coating. The pulse is weak, and the temperature sub-normal. The body weight falls rapidly to much below the normal standard in spite of an appetite which is often voracious *(Diabète maigre)*. Thirst is excessive and micturition is so frequent that broken nights add to the misery of his condition. The quantity of urine varies from 100 to 300 or more ounces in twenty-four hours, and the quantity of sugar ranges from 5 to 10 per cent.

In the *chronic* type the patient is elderly, often florid and well-nourished without any special appearance of ill health, but he complains of unaccustomed weakness, thirst, frequency of micturition and some loss of flesh. Many of these patients have been very stout, so that the wasting is not so apparent (*Diabète gras*). The quantity of urine varies from 60 to 120 ounces, and the quantity of sugar from 3 to 10 per cent.

Prout thought that diabetics were usually fair-skinned and red-haired, and Fagge has confirmed this impression. Such an opinion is of little value, as no one would pretend that all

fair-skinned persons are diabetic or that all dark-skinned persons enjoy an immunity from the disease. Babington believed he could always detect diabetics by their odour. We now know that the breath of diabetics contains acetone and ethylic alcohol at times, but many diabetics do not smell at all differently to healthy persons. The *skin* of diabetics is usually harsh, and the hair dry. The face may be flushed in a peculiar way as if the patient were blushing, or it may be pale, cyanosed, and the lips parched. The nutrition of the *nails* is often interfered with; they become brittle and in some cases come off. The *temperature* is usually normal or sub-normal, but Skerritt has described a case of *acute febrile glycosuria* in which the temperature ranged for three days between 99° and 103°. The intellectual centres are as a rule unaffected; but there is often *irritability of temper* and other evidences of enfeeblement of the controlling centres; common sensation is usually unaffected; motor paralysis is rare, but sometimes occurs as a consequence of diabetic neuritis. The *knee jerks* are frequently absent, probably from the same cause. *Sexual power* is gradually lost; as a rule this loss is permanent, but if the disease improves it may be regained. In females *menstruation* is generally deficient or absent.

Vision is frequently affected, the most common derangement being due simply to weakening of the muscle of accommodation, but toxic amblyopia, retinitis, hæmorrhages, and cataract may occur. *Hearing* is usually normal, though in one of my cases deafness came on at the same time as the disease, and aural complications are not uncommon. *Smell* and *taste* may be blunted. The *appetite* is usually good, and digestion easy, but constipation is very commonly present. The *tongue* is often red and sticky, and the patient usually complains of dryness of the mouth, which sometimes causes a difficulty in deglutition. The *teeth* are generally decayed and falling out, from atrophy of the gums. The abdomen is often retracted, but may present no unusual appearance, and the outline of the liver and spleen are commonly normal, though *enlargement of the liver* is a tolerably frequent occurrence.

The *stools* are peculiarly fœtid; this was first pointed out by Hodgkin who ascribed it to deficient bile.

In uncomplicated cases there is no cough or dyspnœa, and the position and outline of the heart are normal. The *cardiac impulse* is often feeble, and evidences of weak circulation are only too common, especially as the disease advances. *Endo-*

carditis occurs rarely, but *fatty degeneration* of the muscular wall of the heart is a frequent change.

In early cases, before the heart's wall has degenerated, the *pulse* preserves a good degree of tension, as illustrated in *Fig.* 63, which shows a full tidal wave. But later on, the heart fails, the pulse fails too, and we get such a tracing as the following (*Fig.* 64).

Fig. 63.

The pulse rate is not increased unless in consequence of some complication. It is usually regular, without intermissions. A rapid pulse is one of the early signs of the onset of coma.

Fig. 64

The peculiar *odour* of the breath has been already alluded to and ascribed to the presence of acetone and ethylic ether. *Lung* affections, especially chronic phthisis, occur very commonly. The symptoms are very latent, cough being slight and expectoration often absent. But such lung troubles are of the nature of complications and will be fully described in that section.

The *blood* contains excess of sugar, and, as already noticed, its alkalinity is reduced in some cases as much as 50 per cent. Its serum is said to be poisonous to rabbits (ROQUE DEVIC).

Bremer has stated that the red blood corpuscles in diabetes either do not stain or stain very pale yellow, with eosin, but I have not met with this change in the cases I have had examined for the purpose.

Marked anæmia often occurs, in which the red blood corpuscles may be reduced by half and the hæmoglobin by more.

Rollo showed that the blood of diabetics obtained by venesection remained for days without undergoing putrefaction, the sugar acting as an antiseptic. The quantity found has varied in the case of different observers. According to Seegen in mild cases it does not exceed the normal, but in severe examples it may rise as high as 0·4 per cent. Sugar has also been found in the sweat, tears, and saliva.

Very remarkable *fluctuations of body weight* occur during the course of this disease, a variation of two or three pounds being observable in the course of a few days. A patient sent me the following table of weights, and complained that her

medical attendant scarcely seemed to believe in its accuracy. As this experience has occurred to me many times in hospital practice, I do not hesitate to publish it as illustrating a fact.

June 30th	8 st. 13 lbs.
July 7th	9 st. 1½ lbs.
July 14th	9 st. ½ lb.
July 22nd	9 st. ½ lb.
July 29th	9 st. ½ lb.
August 9th	8 st. 12 lbs.
August 14th	8 st. 10 lbs.
August 21st	8 st. 12 lbs.
August 28th	9 st. 0 lbs.
September 5th	9 st. ½ lb.
September 15th	8 st. 11½ lbs.
September 18th	9 st. ¾ lb.

Between the 15th and 18th of September there was a gain of 3¼ lbs. These variations are probably to be attributed to the very great daily loss in water and solids, amounting to many pounds, by which the normal equilibrium of nutrition is deranged.

The Urine.—The capital symptom of diabetes mellitus is the presence of sugar in the urine, and the diagnosis of the disease depends upon its detection.

Is sugar ever present in quantity in the urine of healthy persons? Physiologists tell us that minute traces can be found in normal urine, but the amount is far too small to be detected in the ordinary way.

Flint has asserted that glycosuria, in obvious degrees, is present in one out of three hundred and seventy-seven healthy persons. This statement lacks confirmation, and is not borne out by my experience. The only healthy, or apparently healthy person in whom I have met with glycosuria was the following:—

CASE 37.—*Glycosuria—no polyuria—no thirst—no loss of weight.*

Arthur M., thirty-two, metal roller, came to me in July, 1887, to be examined for life insurance. He was a very powerfully built man, 5ft. 6in. in height, and weighing twelve stone. There was no history of injury, or syphilis, or any family history of diabetes. His knee jerks were present. There was no other evidence of disease but his urine, which was of sp. gr. 1029, and was loaded with sugar. The quantity was not increased. A second sample, examined a fortnight later, was just the same. He was sent again to me in May, 1888, when I found no loss of weight had taken place, and no thirst or polyuria had come on, but the urine was still loaded with sugar, sp. gr. 1023. In order to be sure that there was no fallacy, the urine was fermented and the presence of sugar placed beyond doubt.

I saw him again on February 16th, 1895, when his urine still contained sugar; he weighed 12 st. 9 lbs., and considered himself in perfectly good health.

Eating excess of sugar on an empty stomach causes temporary glycosuria in healthy persons; but it has often occurred to me to ask whether such people are not really dangerously likely to become diabetic, if their power of assimilating sugar is so easily exceeded (FOWLER, COLLINS, von JAKSCH, GROOZ)?

In disease, apart from diabetes, sugar is occasionally found in the urine, but not so often as is sometimes asserted. Thus T. A. Mc.Bride, in a discussion at the New York Academy of Medicine, stated that it may be found in the urine of incipient phthisis, emphysema, chronic bronchitis, chronic pleurisy, heart disease, liver troubles, nervous troubles, cerebral hæmorrhage, fracture of skull, concussion of brain, and in psychoses. He had also met with it in cases presenting the following group of symptoms,—insomnia, neurasthenia, paræsthesia, hemianæsthesia, and paresis. It is very doubtful whether these statements are correct, except for nervous disorders. According to Chovstek alimentary glycosuria can be induced in five out of six cases of Graves' disease. Goodhart has published a number of examples of glycosuria connected with neurasthenia, and the occasional occurrence of this symptom in organic disease of the nervous system and in insanity and epilepsy is sufficiently attested to be indisputable.

The *quantity* of urine in diabetes is generally greatly increased, from 200 to 300 ounces in twenty-four hours being a common amount, but in certain cases, especially in elderly persons, the quantity may not exceed 100 ounces, and where diarrhœa is present may not exceed or may even fall below the normal.

The *specific gravity* is usually high, from 1030 to 1050, but again in elderly persons it may be below 1030, and even below 1020, being only 1013 in two of my cases. A low specific gravity is no proof of the absence of sugar, nor is a high specific gravity any proof of its presence. The *colour* is usually pale greenish yellow, or straw coloured, but gouty diabetics often pass high coloured urine, loaded with lithates. Diabetic urine is generally *clear*, but may be turbid from the growth of torulæ or from lithates.

The *reaction* is almost invariably strongly *acid.*

It deposits very commonly a considerable amount of uric

acid, even in cases in which there is no gout. This is often due to the use of nitrogenous diet. Under the microscope uric acid crystals and torulæ may generally be seen.

Of the normal constituents of the urine there is an increase of water, chlorides (SENATOR), sulphates, creatinin, and phosphates. According to Toralbo the loss of lime in the form of earthy phosphates is so great that it may amount to 2·5 grms. daily. Butel has found that the phosphates stand to the urea as 1 to 10. The urea is increased, holding an approximate relation to the amount of sugar of 1 to 22 (HARRISON and SLATER). The amount of ammonia is greatly increased (HALLERVORDEN). Stadelmann attributes this to the enormous excess of acid in the blood, which in some way disturbs the normal mechanism for fixing ammonia. According to Weil nitric acid is formed normally in the body by synthesis of ammonia, and it is this process which is destroyed, leading to a diminution of nitrates and excess of ammonia.

Of abnormal substances *sugar* is present in quantities varying from 1 to 12 per cent. It has been suggested that where vesical catarrh is present the sugar may be destroyed by a process of fermentation in the bladder, and F. Müller has related a case of pneumaturia in which the bladder contained a mixture of carbonic acid, hydrogen, and nitrogen, derived, he believes, from fermentation of sugar which was present in the urine; but as Teschemacher points out, if this were the case alcohol should be formed, and so far this has not been demonstrated. Glycogen is said to be constantly present (LEUBE), and lævulose in some cases (SEEGEN).

For a time the sugar may be present intermittingly, as in the following curious case :—

CASE 38.—*Diabetes Mellitus—thirst—polyuria—intermittent glycosuria—rheumatic pains—lichen scrophulosorum—scaly eruption on scalp—amblyopia—ultimate death from coma.*

George B., aged twenty-eight, was first admitted on July 24th, 1886, complaining of lumbar pains, thirst, and polyuria.

History.—The last two symptoms had existed for three months, but the pain for only three weeks. At Christmas he had *rheumatic* pains in feet and knees, but was not confined to bed, and had never been well since. He could remember no other illness, or any injury. His family history was good, and he knew of no other case of diabetes among his relatives. He had been under treatment by Dr. Foxwell as an out-patient for three months, before his admission. His urine averaged over 200 oz., sp. gr. 1040; urea 0·9 per cent.; sugar, 8·0 per cent.; he had lost 14 lbs. in weight. He was sent to the Suburban Hospital and afterwards re-admitted

from there on September 26th of the same year. He then complained chiefly of weakness.

Condition on Admission.—He was a fairly well-built and well-nourished man, with a pale and anxious face. He weighed 8 stone 9½ lbs. There was slight ptosis of the right eyelid which had always existed. His skin and joints were normal. Patellar reflexes present. Tongue clean. Bowels confined. No abnormal physical signs. Pulse, 66; Temp., 98°; Resp. 24. On ordinary diet he passed over 100 oz. of urine, but on being put on diabetic diet the quantity fell to 50 to 60 oz., while the sugar fell from 8 per cent. to 1·1 per cent. There was generally a faint haz of albumen present.

Progress of Case.—He was treated with Clemens's solution, and under this treatment the urine kept low, the sugar was never more than 4 per cent., often much less, and he gained weight. On his discharge, November 2nd, he weighed 8 stone 12½ lbs. He was made an out-patient.

After leaving the hospital he attended as an out-patient, continuing his diet as well as he could, and going on with cod-liver oil and iron. After this his urine was often free from sugar for months together, even though he ate bread.

On November 13th the urine had a specific gravity of 1035, but contained so little sugar that it was analysed in order to find out what solid constituent was in excess, and 4·5 per cent. of urea was found to be present. He complained about this time of bleeding from the gums, which was stopped by a krameria mouth wash.

On December 4th, he had an eruption of lichen scrophulosorum on the chest, which was soon cured by ung. hydrarg. ammon.

Jan. 1st, 1889. His urine contained sugar, and continued to do so in varying amounts. In February he complained of a dry, brown scaly eruption on his scalp, which was greatly improved by washing with borax lotion. He began to complain of dimness of vision, and on May 28th he was sent to the Eye Hospital for a complete report upon his vision, which was as follows :—

V. in R. eye is $\frac{5}{30}$ when corrected for error of refraction; V. in L. eye is $\frac{5}{20}$ badly. Both fundi are normal, and media clear. He smokes over 4 oz. of black twist tobacco a week, and has central scotoma for red and green, the defect arising no doubt from toxic amblyopia. Sees better in twilight, etc.

This patient died of coma, on Nov. 10th, 1891. His lungs were tubercular, and his blood very fatty; his pancreas was atrophied and soft. When re-admitted he had well-marked physical signs of consolidation and excavation at the right apex. He looked anæmic and his blood showed—Red corpuscles, 2,700,000; White corpuscles, 8,000; Hæmoglobin, 50 per cent.

Albumen is occasionally met with in the urine of elderly diabetics; it is less common in young subjects. Maguire says he has always found it in the urine of cases of diabetic coma of Küssmaul's type. This is generally true, but there are exceptions to this rule.

Indican and skatoxylsulphuric acid may be present in excess (OTTO).

Acetone, aceto-acetic acid, beta-oxybutyric acid, and beta-crotonic acid have all been found in the urine, and stand in close chemical relation to one another. Much interest attaches to these bodies, as they are believed to be the poisons which give rise to Küssmaul's coma, and some of them give the well-known Burgundy red coloration with ferric chloride. This reaction is also occasioned by formic acid, which, according to Le Nobel, is present in diabetic urine. Oxalic acid and hippuric acid are also frequently present (CZAPEK).

Tests for Sugar.—These will be found in full on p. 197, *et seq.*, and need not be repeated here.

Tests for Acetone.—(See p. 200.)

The Ferric Chloride Reaction.—(See p. 201.)

PROGNOSIS.—As a general rule the prognosis of diabetes depends upon the age of the patient. Under forty it is a fatal, and usually a rapidly fatal disease. Over forty it is chronic, often intermittent, and sometimes curable.

But in considering this very important question the etiology of the disease should always be carefully studied and duly considered. Harker's case of a child of two years of age, who recovered, was apparently due to excessive use of sugar with his food. A family tendency to diabetes, or to nervous affections, is a bad prognostic element. On the other hand, many recoveries have taken place where the disease has supervened after an injury, or some acute disorder, such as diphtheria. Probably the most favourable cases are those which are distinctly related to obesity or gout, especially where the glycosuria is intermittent, and the quantity of urine not very large. Climacteric diabetes is also held to be eminently curable.

The third consideration that must always guide our prognosis is the progress already made by the disease; the degree of emaciation, the quantity of urine, and the total quantity (not the percentage) of sugar excreted; in other words the earlier the case comes under treatment the better.

The fourth point is the influence that dietetic restrictions are found to possess in controlling the excretion of sugar.

Fifthly, much depends upon the conditions under which the patient lives, for in this as in so many other chronic diseases, freedom from care and anxiety, and the possession of the means to secure the most favourable advantages of climate,

residence and diet, count for much in prolonging life, even if a cure cannot be obtained.

But diabetes under no circumstances can be regarded as free from danger. The elderly diabetic, whose symptoms can be easily controlled, is liable to die suddenly from some slight imprudence, and is never out of risk. The presence of albuminuria, acetonuria, or diaceturia is only a danger signal, and does not make the prognosis necessarily worse (SCHMITZ).

DURATION.—It is true, as a general statement, that diabetes runs a longer course in direct proportion to age. In other words, it is an acute and rapidly fatal disease in children and young persons, lasting only weeks or months, or perhaps a year or more. Nevertheless, I have met with cases in children that seem to run a very chronic course; and Pavy has related instances lasting five, eight, and even more years. Agnes L. was seen last in 1894, and had then been ill eight years; she was fifteen, and looked like a child of six or seven.

On the other hand, in elderly persons the disease lasts for years. Worms has given instances where it lasted from twelve to twenty-five years, and disappearance of the symptoms is not uncommon.

TERMINATION.—Death occurs in many cases as a result of one or other of the complications to be described, of which pneumonia and pneumonic-phthisis are the most common. In very many cases the patient's strength is gradually reduced, and he dies quietly in a drowsy state without being actually comatose. But in a large proportion death is more or less sudden, the fatal symptoms supervening as the result of some slight occasioning cause, such as a walk too great for their enfeebled powers, a chill, excitement, etc. In these cases death is preceded by coma. This mode of death is so peculiar that it has attracted much attention, and will be described in a separate chapter.

COMPLICATIONS.

INTEGUMENTARY SYSTEM.—The skin of diabetics is generally dry and harsh, with not uncommonly a tendency to desquamation of the epidermis. The circulation may be feeble, and there is often some cyanosis of the ears, nose, and cheeks, while the feet and legs are cold. *Acne pustules*, *boils*, and *carbuncles* occur not infrequently in elderly diabetics. Pigmentation of the skin, especially marked on the exposed

surfaces may occur in the type called bronzed diabetes. The most common skin affection is a form of *erythema* on the hands and arms, legs and feet. The patches are slightly raised, irregularly oval in shape, about half to three quarters of an inch in their longest diameter, and purple in colour.

CASE 39.—*Diabetes Mellitus—very slight polyuria—thirst—hunger—erythematous eruption on extremities—cataracts—deafness—sciatica—diarrhœa.*

Elizabeth R., aged thirty-seven, shopkeeper, was admitted into the General Hospital on May 30th, 1889, complaining of weakness of the arms and legs, thirst, and polyuria, with pain in the back and abdomen after food, and an eruption on the nape of the neck and on the feet; also of failing sight. She had been quite well up to four years ago, when, being pregnant for the second time, she suffered from thirst and swelling of the legs, which continued after her confinement, and she became weaker and thinner. She kept a mangle and a little shop up to four months ago, when her parents took her home to live with them.

Family History.—Her own mother died of phthisis, but she had a step-mother. Her father was alive and in good health, but very nervous. Two brothers and a sister were alive and well. Patient was a widow, her husband having died of bronchitis two years ago. She had had two children, both dying after a few weeks of life.

State on Admission.—She was fairly developed, but greatly emaciated, skin dry, some patches of eczema with enlarged lymphatic glands in the nape of the neck, due to *pediculi capitis*. Skin of lower part of legs and feet roughened and mottled with irregular discoloured areas of congestion, varying in size from a sixpence to a shilling, which itched when warm. These had been coming out in successive crops for eighteen months. The spots when fresh were raised above the general surface of the skin. Temp., 97·6°; pulse, 96; Resp., 20. Weight, 5 st. 8½ lbs. She thought the quantity of her water was about eight pints; and a specimen examined was clear, acid, 1026, pale brownish-yellow, loaded with sugar, and containing a faint cloud of albumen.

On June 1st, three days after admission, the urine report was as follows:—68 oz., 1020 acid, pale opalescent; urea, 0·9 per cent.; sugar, 2 per cent.; albumen a very faint haze, blood in traces. Under the microscope, red and white blood corpuscles and squamous epithelium. The blood and albumen were thought to be due to the vaginal discharge. This was on milk diet with bread.

Treatment.—She was then put upon the following diet:—Meat, green vegetables, a pint of beef tea, gluten bread, Vichy water and lemon juice. She was ordered, in addition, a teaspoonful of cod liver oil three times a day.

July 16th. For the last three days there had been slight swelling of the eyelids with watery discharge, and there was some conjunctivitis with a small sub-conjunctival hæmorrhage in the right eye.

This morning an extensive eruption broke out over the forearm and hands. It consisted of rose-coloured elevated spots, as large as a split pea, thickly distributed over the elbows, fingers, and palms of the hands, and often coalescing so as to produce red shiny blotches. Some of the larger spots had a tendency to become white and transparent in their

centres, looking something like nettle stings. This papular erythema gradually faded until by the 22nd there was only a brownish-red mottling over the seat of it. Shortly after this she was made an out-patient (July 24th).

Leroux has described the case of a child in whom a symmetrical erythema in large elevated itching patches attacked the nose and chin. This was followed by an outbreak of psoriasis guttata. Later on the nails underwent a peculiar change, which led to their falling off, and finally, after copious sweating, a lichen-like papular eruption appeared, which was followed by numerous boils. Davies Pryce has described a condition which he has called erythematous œdema; he believes it to be dependent upon diabetic neuritis. It is characterised by very severe gnawing pains, with swelling and discoloration of the skin. *Burning* of the palms of the hands and soles of the feet (MARCET) may be complained of, while sweating in the same situations is not uncommon. Profuse general sweating sometimes occurs, as in a patient of mine, a male, aged thirty-nine, in whom it was checked by Dover's powder after atropine had been tried and failed.

Bronzing of the skin, so as to suggest Addison's disease, is seen in association with a peculiar pigmentary cirrhosis of the liver, under which it is described (*see p.* 321).

Eczema of the genitals is somewhat common, especially in women, and may constitute a serious trouble. It is undoubtedly set up by the irritation of fungoid growths in the saccharine urine remaining on the parts, and in males a very little cleanliness will prevent this. Even in men, however, an eczematous balanitis may occur. In women the difficulty of keeping the parts thoroughly clean is greater, and eczema attended by great irritation, which spreads over the abdomen and thighs and renders life a misery, is too often seen. In some cases *pruritus* vulvæ is complained of without any eczema being present. *Purpura* may occur in the earlier stages (SIMON). Horden has recorded a case of *pityriasis rubra* in a diabetic.

Kaposi has described an affection to which he has given the name of *papillomatosis diabetica*. The patient was a Brazilian doctor, who had suffered from diabetes for twenty years, but was well-nourished and vigorous. The affection was limited to the left arm and forearm which were extensively swollen, and the backs of the fingers were covered with excrescences varying in size from a lentil to a sixpence, ulcerated in places,

the ulcers being rounded or kidney-shaped, bordered by florid granulations, and discharging freely. On the elbow was a growth as large as the palm of the hand, raised over two centimetres above the level of the surrounding skin, deeply fissured and presenting a slightly bleeding surface covered with warty protuberances.

Addison and Gull first described a peculiar eruption which is now called *xanthoma tuberosum.* A case was described by Dr. Bristowe in 1866. In his case the eruption consisted essentially of somewhat indurated tubercles of a dull reddish hue (but not much deeper in colour than the surrounding skin in their neighbourhood) and of roundish or obtusely conical form. Their margins passed invariably into the healthy skin around, and their apices were often of a pale yellow colour, as though containing a minute quantity of pus. Their size was not uniform; to speak roughly their horizontal diameter varied from a line upwards, and their vertical projection from a line downwards. The yellowness of their apices was found not to be due to any accumulation of fluid there; for this part, like the rest of the tubercles, was quite solid. The tubercles appeared from microscopical examination to consist essentially of a kind of dense fibrillated texture, studded more or less with oil globules of various sizes. It was the presence of such globules in great abundance that caused the yellowness just described.

Marchal (de Calvi) quotes a case, perhaps of this nature, where the body of the patient was literally covered with great coppery pustules or hard vesicles, containing a material as hard as very dry cheese. They were harder and more elevated than variola pustules. Some were rounded, terminating abruptly in a point. Generally isolated, they were occasionally in groups. This eruption disappeared, leaving only minute cicatrices, and did not recur as the disease got worse.

This tendency to disappear is true of xanthoma.

Another peculiar eruption, in the form of circumscribed necrotic patches, has been described by Rosenblath. It occurred in the form of small round red spots the size of pins' heads, about the ankles and on the dorsum of the feet. Some of the spots were little vesicles containing watery fluid. At the autopsy they were found to consist of little centres of necrosis, and ulceration was found on the tongue and in the mucous membrane of the œsophagus, stomach, and intestines. The skin eruption appeared to commence in the sweat glands.

Cellulitis and *gangrene* are complications which are more apt to occur in diabetes as life advances, and are more common in men than in women, though Hunt throws doubt on this latter statement. Godlee thinks that gangrene in diabetes is due to two distinct causes requiring different treatment. In the first the condition depends upon arterio-sclerosis, and amputation should be performed high up, but in the second, where it is caused by neuritis, he counsels abstention from operative interference.

CASE 40.—*Diabetes Mellitus—perforating ulcers—gangrene of both lower extremities—successful amputation of necrosed parts.*

Joseph F., sixty-four, tailor, was admitted February 20th, 1889, with gangrene of right foot.

History.—Father died at eighty-six; cause not known. Mother was killed. Three brothers alive; one brother died young. No history of illnesses. About five years ago he came under Mr. Chavasse with what he called "corns" on the second digit of each foot. That of the left foot got well, and the toe on the right foot was amputated. At that time he had no suspicion of any illness. He had not complained of thirst or of weakness; but on coming to the Hospital he was told he had diabetes. For some time he was only slightly troubled with sores on his toes, and about eighteen months ago he began to be thirsty. Twelve months ago last March all the toes on the left foot were taken off in the General Hospital, and he then went to the Suburban Hospital, leaving there in July. In January of this year the toes on the right foot began to be affected, and in February he came into the General Hospital again, and the third and fourth toes were amputated at different times. In April the ankle began to be bad, and on June 15th the leg was amputated. Latterly his health has not been so well. It is only in the last twelve months he has noticed he has been passing a large amount of water. Has had no cough. No history of boils or other skin diseases.

Whilst the urine was measured from April 3rd to 21st he was passing from 66 oz. to 109 oz in twenty-four hours, with an average of about 90 oz.

Urine Report:—

Feb.	25.	—	1036.	Acid	Urea	1·4	p.c.	Sugar	8·3	p.c.	Acetone none.
Mar.	29.	—	1036.	„	„	·8	„	„	5·5	„	„ present.
April	1.	70 oz.	1034.	„	„	·5	„	„	5·2	„	„ „
„	6.	88 oz.	1030.	„	„	—	„	„	5·5	„	„ „
„	15.	80 oz.	1036.	„	„	—	„	„	5·0	„	„ —
June	17.	—	1033.	„	„	1·0	„	„	6.2	„	„ —

CASE 41.—*Diabetes Mellitus — polyuria — thirst — albuminuria — gangrene of toes—knee jerks diminished—improvement on diet and opium.*

William F., aged fifty-seven, attended as an out-patient on October 26th, 1886, complaining of passing three to four quarts of water and of getting up very frequently at night for this purpose. He had been ill three years, when he got gangrene of three toes on the right foot, and his urine was found to contain sugar. He suffered from thirst; his urine was pale, clear, sp. gr. 1022, and contained a cloud of albumen and a large quantity

of sugar. The knee jerks in both legs were almost absent. On anti-diabetic diet and opium he lost his thirst, he was not disturbed at night to make water, and the quantity of this secretion fell to 90 oz. daily, or little more than two quarts, of sp. gr. 1020. He was not seen after January 18th, 1887.

Kaposi has described a rare condition under the name of *gangræna bullosa serpiginosa.* The patient was a woman, aged fifty-one; on her left leg were three gangrenous patches, and over the neighbouring sound skin fifteen or twenty bullæ varying in size from a pea to a bean. The condition improved somewhat under treatment at Carlsbad, then got worse and the patient died.

Several cases of *perforating ulcer* of the foot in diabetes have been published (Kirmissen, Heusoner, Spencer). The ulcer is preceded by circumscribed anæsthesia, and an anæsthetic zone surrounds the ulcer when formed. In Heusoner's case the ulcer preceded the symptoms of diabetes, and *post mortem* nothing abnormal was found in the medulla or pons. It is probable that this lesion is another consequence of disease of the peripheral nerves.

Against this formidable catalogue of skin affections due to diabetes it is some comfort to set the fact that persons have been known to lose chronic skin affections upon the supervention of diabetes (WATSON).

Kaposi attributes all diabetic skin affections to impregnation of the skin with sugar. We have seen that in the case of eczema genitale, the sugar is undoubtedly the exciting cause, but its direct influence is doubtful in other cases. We know that all the tissues of diabetics are very prone to disease in consequence of malnutrition, but it is taking a somewhat narrow view to ascribe everything to the sugar circulating in the blood, which not unfrequently is not more than normal, the overplus being constantly excreted by the kidneys.

Dropsy.—In a disease characterised by polyuria it is hardly to be expected that dropsy should occur. It is, however, sometimes present, evidently as a result of heart failure and is attended by a cessation of the polyuria. Ascites may be present as well as œdema of the lower or even upper extremities (ROBERTS).

CASE 42.—*Diabetes Mellitus—bronchitis—œdema of trunk and lower limbs—recovery.*

Mary Ann M., aged thirty-nine, widow, metal button maker, was admitted into hospital on January 8th, 1887, complaining of cough, pain in the back, and swelling of the legs and abdomen.

History.—She had been ill six weeks, the attack commencing with cough. A week ago she noticed her abdomen was swollen, and soon after the legs began to swell. Her breath got very short, and she felt very ill and weak, but she went about until the day of admission. She had been quite strong, except that ten years ago she had rheumatic fever, and for the last five or six years had suffered from a cough in the winter.

Condition on Admission.—There was much cyanosis of the face, hands, and arms, with great œdema of the lower extremities and trunk, but no ascites or hydrothorax. She could not lie down in bed, and her breath was very short and wheezy. Pulse 114, Temp. 98°, Resp. 30. Troublesome cough; no dulness over lungs: breath sounds very wheezy, with moist râles and sibilant bronchi throughout; vocal resonance undiminished; heart's action regular, no murmur; pulse very small and weak. She had not menstruated for two months, and the flow had been very scanty for some months. Urine 48 oz., acid, 1043, a faint cloud of albumen, 8·3 per cent. of sugar, no blood, no casts, squamous and pear-shaped epithelium in deposit.

She was put on strict anti diabetic diet, with a little morphia for her cough. On this treatment she steadily improved, the sugar diminished rapidly, and the œdema disappeared. She left the hospital on February 21st, free from dropsy and with no sugar in her urine, though this still showed a faint trace of albumen.

TEMPERATURE.—The temperature in diabetes is usually normal or sub-normal, and in some cases may be very low indeed, as in the example given by Fagge, where the thermometer marked only 93·6. In the following case the temperature was irregular, being sometimes as high as 100°, sometimes as low as 95°.

CASE 43.—*Diabetes Mellitus—polyuria—wasting—diarrhœa—very low temperature—discharged unrelieved—subsequent death.*

George H., forty-two, tailor, was admitted into hospital on Jan. 25th 1887, complaining of tingling of his tongue and the roof of his mouth, with cramps in his legs. These symptoms came on about a week after Christmas.

History.—He had been losing weight since November. He had been passing more water than usual and had been thirsty. He had never been ill, except that when he was nineteen he spat a little blood. Father died aged thirty-five of "brain fever"; mother died aged seventy, of "diseased stomach." There was only one sister, who died when she was five, but he did not know the cause of death. He had never met with any accident or personal injury.

Condition on Admission.—He was a poorly nourished man. Pulse 90, Temp. 100°, Resp. 17. Physical examination revealed nothing, except some want of resonance and deficient breathing at the apices of both lungs, and his pulse was very weak. Urine 116 oz., sp. gr. 1035, acid, straw-coloured, no deposit; 0·8 per cent. of urea, 5·8 per cent. of sugar, no albumen.

Progress of Case.—He was dieted and treated with alkalies and cod liver oil; afterwards with morphia. He had several attacks of diarrhœa which interfered with his progress, and his temperature was irregular, sometimes

rising to nearly 100°, *but more often being sub-normal, being several times as low in the morning as* 95°. The low temperature was not the result of the diarrhœa, that is, it did not occur at the same time as the diarrhœa, or after those attacks. He never complained of feeling cold when it was at its lowest, and on being asked said he did not feel cold. He was ultimately discharged, and we heard died in a short time.

DISAPPEARANCE OF GLYCOSURIA.—In acute febrile diseases the sugar sometimes disappears from the urine, as in a case of enteric fever, reported on p. 322. It has also been observed to disappear in relapsing fever (SIMON), small-pox (RAYER, PAVY), febrile angina, dysentery (ANDRAL), and pneumonia (LEUBE, OLIVER). Dr. Nöel Paton has shown that in animals glycogenesis is increased by diminished elimination of heat, but diminished by fever caused by the products of bacterial growth. Bernard noticed the absence of glycogen from the livers of fever patients.

NERVOUS SYSTEM.—The connection between diabetes and grave diseases of the nervous system has been fully illustrated in the section on etiology, it is, therefore, not surprising if in this disease we meet with listlessness and depression of spirits, weakness and peevishness of temper (WATSON), or even melancholia with suicidal tendencies (LEGRAND DE SAULLE), or temporary mania (PAVY). In certain cases there seems to be an alternation between the mental disturbance and the glycosuria, the latter only appearing when the patient's mental state is relatively good (MADIGAN).

In some cases there may be symptoms resembling those due to an intra-cranial growth, *e.g.*, headache and giddiness, with epileptic or apoplectic attacks.

Diabetic *neuralgia* is usually symmetrical, though it may commence on one side. It usually comes on suddenly, frequently in bed, and the pain is excruciating. Each attack lasts only a short time, but there may be three or four in twenty-four hours. The attacks appear to be aggravated by the warmth of the bed. The sciatic nerves are specially liable to be attacked (CORNILLON).

CASE 44.—*Bilateral Sciatica—glycosuria—albuminuria—no polyuria or thirst.*

Ebenezer H., sixty-five, came as an out-patient on May 14th, 1889, complaining of paroxysms of excruciating pain in the course of the sciatic nerves.

History.—He said the attacks lasted six to eight hours, and that they had come on about once in three months for the last twenty years. For thirty years he had been subject to attacks of gout. He did not know of any case of diabetes in his family.

Condition on Admission.—He was a short, stout, florid man; he had lost most of his teeth; his bowels were confined. Physical signs normal. Urine, sp. gr. 1013, acid, a cloud of albumen, reduced Fehling moderately. He was dieted, and ordered to take the following:—

℞ *Sodii Salicylatis* gr. xv.; *Infusi Gentianæ* ℥j.; to be taken thrice daily.

May 28th.—The urine was free from sugar, and there had been no more paroxysmal pain.

CASE 45.—*Diabetes Mellitus—thirst—polyuria—wasting—unilateral sciatica.*

Josiah W., fifty-six, came to the out-patient department on April 1st, 1886, complaining of pain and swelling in the right leg, which he had been told was sciatica. He also complained of violent pain in the abdomen, of great thirst, and of passing a large quantity of water, as much as three pints in the night alone.

History.—He had been under treatment for six weeks, but the pain began a month earlier. He had been losing weight. He had usually enjoyed good health, but eighteen years previously he had "rheumatics," and was laid up five weeks, with pains which shifted about; his knees were swollen at the time. He had bronchitis twelve years ago; he had never had gout. Had a comfortable home; said he was temperate, but drank two or three pints of beer daily. He used lead in his work to hold castings, but there was no lead dust. Father died, aged sixty-three, of apoplexy. Mother died, aged sixty-three, of dropsy. Of his thirteen brothers and sisters five were living in good health; the others died in infancy, except one sister who died in childbirth.

Condition on Admission.—He was a big, stout man, with a florid face; weighed 14 st. 3 lbs. No blue line on gums. Right leg pitted on pressure, but there was no obvious swelling, except some puffing over the instep. No œdema elsewhere. Pulse 88, Resp. 18, Temp. 98·8°. Physical signs normal. Breath foul; tongue red at edges; suffered from wind; bowels regular. Urine 76 oz., loaded with sugar, a cloud of albumen.

Progress of Case.—He was put on diabetic diet with an alkaline mixture, and the sugar at once disappeared. The pain rapidly improved. On being allowed ordinary diet, the urine contained 2 per cent. of sugar, which disappeared again at once on the diabetic diet being resumed. The swelling and pain completely disappeared, and before he left he was allowed a little brown bread, without giving rise to any return of glycosuria. He was discharged on May 5th, and made an out-patient.

Florain has described a painful affection of the fingers, like the *pricking* of a pin, which occurred in a pregnant woman whose urine was loaded with sugar. Intense hyperæsthesia of the soles of the feet has been described by Auerbach.

Loss of sexual desire is an early and very frequent symptom.

Paralysis may attack single groups of muscles, giving rise to *ptosis*, *strabismus*, or *paralysis* of a limb. This is probably not due to central disease, but to peripheral neuritis, examples of which have been published by Althaus and Buzzard.

Mabboux thinks that conjugate paralysis of the ocular muscles is generally diabetic in origin. In other cases there may be complete *paraplegia*, affecting both upper and lower limbs, mobility, sensibility, and reflexes being all abolished, without paralysis of the sphincters (STRAHAN). This form is also evidently due to general peripheral neuritis. In some cases there may be symptoms closely resembling *locomotor ataxy*, and although the pupil reflex was said to be never lost (FISCHER), Grube has shown that this is unfortunately not always true. The last author has also described gastric crises closely resembling those of tabes as occurring in diabetes.

Salomonson has described a case in which, after violent exercise in skating, the patient complained of pains in the body and legs. Sensibility and gait were normal, and there was no loss of co-ordination, but the superficial reflexes were impaired, and the patellar reflexes on both sides were abolished. She could stand with her eyes shut, and the pupils reacted well to light. The right eye was healthy; the left showed some opacity of the lens. There was great diminution of the galvanic excitability of the muscles and nerves. He regarded it as a case of peripheral neuritis due to diabetes.

Davies Pryce has described three very good examples of this pseudo-tabes of diabetes; they all occurred in elderly people with well-marked arteriosclerosis.

CASE 46.—*Diabetic general neuritis.*

T. G., aged 60, engine driver, admitted into the General Hospital February 19th, 1896. He had been suffering from diabetes, particularly from thirst and loss of flesh and strength for two years. Lately, his eyesight had grown dim from the formation of cataracts; one eye was operated on unsuccessfully, panophthalmitis resulting. A fortnight before admission he found both arms painful and numbed, and every day they became more powerless. On admission, he was found to be passing three to four quarts of water of sp. gr. 1038, containing about 5 % of sugar; no reaction of acetone or with liq. ferri perchlor. His breath had a sweetish odour, and his mouth was dry. Except weakness of the heart's sounds, there were no noteworthy alterations in the physical examination of the thorax and abdomen. The muscles of the extremities were wasted and flabby, and he could walk with difficulty; he could raise the right arm from the bed, but not the left, and had no power of gripping in either hand. The hands looked puffy, smooth and shiny. He complained of numbness in his fingers and toes. Common sensation was greatly diminished in both arms and hands, and there was great blunting of the sense of pain in both arms and in both legs below the knees. Sensation of heat and cold was absent in the same areas, and over the rest of the body was delayed and imperfect. The knee jerks were entirely absent,

but the plantar reflexes were increased and the other superficial reflexes were normal; organic reflexes normal. In the right arm the flexor muscles did not respond at all to faradism, but the extensors contracted well to a strong current; in the left arm no response was obtained to the strongest current from any muscle; electro-sensibility was absent. Both arms failed to respond to the galvanic current. Below the knees there was no faradic or galvanic response, but above the knees the muscles reacted well to a strong faradic current. There was some tenderness over the trunks of the musculo-spiral nerves in both arms, but none over other nerve trunks. He was dieted and carefully nursed, but grew worse. His urine had to be drawn off by a catheter and became purulent and ammoniacal. He passed his fæces at times in bed—apparently from mental dulness. He was at times delirious, and wanted to get out of bed at night. On the afternoon of March 2nd, he had a rigor; his temperature rose to 100°, and his pulse became almost imperceptible. He died the same night.

The *post mortem* examination showed the body to be much wasted, and the muscles of the legs, upper arms, and forearms very flabby; there were

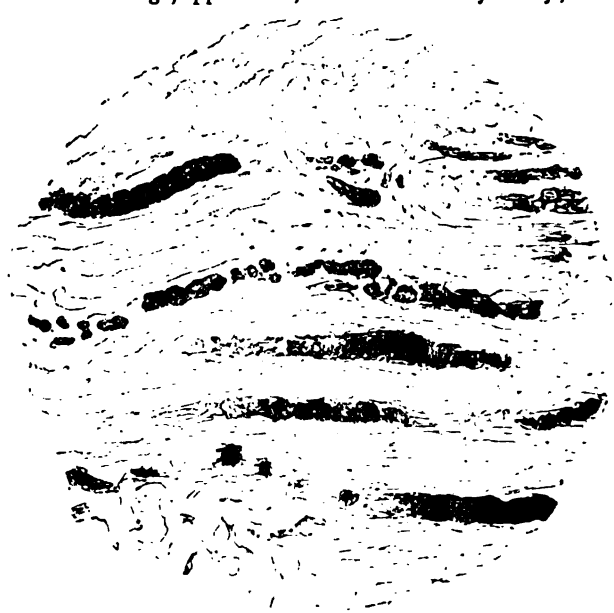

Fig. 65.—Right Median nerve, showing very advanced interstitial and parenchymatous neuritis. Osmic acid preparation.

bed-sores on the ankles, trochanters and sacrum. The pericardium was adherent to the *heart* by fine fibrous tissue; the myocardium was pale, tough, and in parts had undergone fibroid degeneration; the coronary arteries were narrowed and calcified, and the mitral and aortic valves were thickened and rigid. The *lungs* were adherent, emphysematous, and

engorged. The *stomach* was dilated; the *liver* weighed 80 oz., was enlarged, brown, soft and fatty. The *pancreas* weighed 6 oz., was indurated and gritty on section; the kidneys were enlarged, together weighing 17 oz., dark red, cortices broad, pyramids atrophied at their apices, calyces and pelves dilated and catarrhal; the *bladder* showed traces of cystitis. The *suprarenal* bodies were enlarged and degenerated; the *spleen* was soft and pulpy. The *brain* weighed 46 oz.; its cortex was atrophied, sulci widened, pia mater and arachnoid thickened and opaque. The carotids showed extensive atheroma, and the basilar was filled with clot which could not be squeezed out. The *spinal cord* showed no naked eye changes, but under the microscopes the cells of the anterior cornua were swollen and pigmented. The *peripheral nerves* were partially examined; the right median nerve showed (*Fig.* 65) extreme interstitial neuritis with great increase of connective tissue forming broad bands in which no nerve substance was visible, and the nerve fibres themselves showed an advanced degree of segmentary degeneration of their myelin sheaths; the same description applies to the state of the left median nerve, the right radial, both anterior tibials, and in a less degree to both sciatics.

Lépine and Blanc have described a case of hemiplegia with only microscopic lesions in the motor convolutions.

Apoplexy occurs sometimes, but is not common.

CASE 47.—*Diabetes Mellitus—no polyuria—wasting—vertigo—albuminuria—apoplexy—death.*

Mr. W., fifty-six, was seen in 1885, as a candidate for life assurance, when sugar was found in his urine. He was brought to me on Nov. 29th, 1886, by Mr. F. W. Underhill, of Moseley, complaining of giddiness and temporary attacks of loss of consciousness. His eyesight was good; there was no hemiopia, or double vision; his optic discs were normal. There was no obvious hypertrophy of the heart; the pulse was rather empty. The urine was not increased in amount; he did not rise at night to pass it; it was acid, sp. gr. 1021; contained a little sugar, and gave a haze of albumen on boiling.

I heard that he got much better on the treatment employed; but on Feb. 3rd, 1887, he had some friends to dinner and drank champagne. The following day he was seized with deafness, inability to speak, and progressive stupor. When seen late that night he could not speak, his pupils were contracted, his pulse hard, and he was restless; but there was no paralysis of the limbs. He was bled to 16 oz., and afterwards expressed himself by signs as feeling better. However, he died the following night from œdema of the lungs.

Coma occurs frequently as the termination of diabetes, and will be described separately.

Epileptic Fits occur occasionally.

Finlayson has described a case in which repeated fits alternating with furious mania occurred for seventeen hours before death. The urine was quite free from albumen, and on *post mortem* examination there was nothing to account for the convulsions.

Loss of Knee Jerk has been observed very commonly in diabetics; it is attributed by Strumpell to degeneration of the peripheral nerves. Dreyfous has met with an example of exaggeration of the knee jerk in a diabetic woman aged sixty-eight. According to Bouchard it was absent in nineteen out of sixty-six cases, or in 29 per cent. Of those in which it was absent 6 or 31·5 per cent. died, while of the others only 2 or 4·2 per cent. died, which suggests that absence is of very bad prognostic significance. Still it is said that the jerk may reappear if the symptoms improve (MARIE and GUINON). Rosenstein does not agree in regarding the loss as of grave import, as he found that it bears no relation to the amount of sugar or to the acetone or ferric chloride reaction-giving substances in the urine. He points out that it cannot be reproduced by subcutaneous injections of strychnine, as in alcoholism. Grube also disputes the significance of loss of knee jerks. He examined 113 cases; of these, the knee jerks were—

Normal	in	113
Increased	„	5
Diminished	„	13

Of the last there were—

Severe cases		4
Slight	„	9

so that he concludes that the absence is of no importance, and in this I agree with him.

Barnes has described a case in which the symptoms of diabetes and *exophthalmic goitre* came on simultaneously. The patient was a domestic servant, aged thirty-four; she died after being under observation about three months, but unfortunately no examination of the body could be obtained.

EYE AFFECTIONS.—The table on the next page of one hundred and forty-four cases, collected by Galezowski, shows the relative frequency of various eye affections in diabetes.

He thinks of these, cataract, retinitis, amblyopia, hemiopia, and muscular paralysis, alone, are to be regarded as really dependent upon diabetes; the others are merely accidental complications.

Deutschmann has found in diabetic eyes swelling and softening of the pigment layer on the posterior surface of the iris. In the deepest layers of the lens he found leucocytes containing myelin, with irregular lumps of albuminous material lying between the lens fibres and fine granulation and vacuo-

DISEASES.	CASES.	PERCENTAGE.
Conjunctivitis and Disturbance of accommodation	5	3·5
Keratitis	4	2·8
Iritis	7	4·9
Choroiditis gummatosa	4	2·8
Cataract	46	31·0
Retinitis	27	19·0
Amblyopia	31	21·7
Hemiopia	4	2·8
Paralysis of ocular muscles	10	7·0
Detached retina	3	2·1
Atrophy of optic nerve	3	3·1

lation in the peripheral fibres, the epithelium of the anterior capsule stained irregularly, with granular degeneration of the nuclei both at the equator and the periphery. He thinks the changes in the lens depend rather upon the general malnutrition than upon the presence of sugar.

Diabetic Cataract is bilateral, developing and ripening quickly; it occurs in younger persons than ordinary cataract, and is attended by severe symptoms of diabetes. It was noticed by Mackenzie and Duncan, but was first clearly described by France in a paper in the *Ophthalmic Hospital Reports* for 1859. These cataracts are usually soft, but not always (GRAEFE, WILDE), and they may disappear spontaneously (NETTLESHIP). Operations for their removal are generally undertaken on young subjects, but these are not free from danger, as there have been several cases of death from coma following this operation (SPENCER), and the healing process is liable to disturbance by attacks of iritis, etc., (SAMELSOHN).

Diplopia is mentioned in a case recorded by Willan and quoted by Rollo; it is due to paralysis of the external rectus on one side. A more common condition is amblyopia, depending upon paralysis of the muscle of accommodation, with loss of converging power, which Trousseau was the first to point out as an early symptom of diabetes. It may be only temporary, passing off after a time (WALLACE ANDERSON).

CASE 48.—*Diabetes Mellitus—brought on by an attack of influenza—amblyopia from failure of accommodative power—pruritus vulvæ.*

O. M. B., aged twenty-two, single, housemaid, was admitted into Hospital on April 15th, 1890, complaining of great hunger, thirst, and

polyuria. Her illness had lasted about three months. Just before Christmas she went to the Eye Hospital on account of inability to read.

History of Present Illness.—Some time before last Christmas she had an attack which she called influenza; it lasted about a fortnight, and left her very weak. Soon after this she noticed that she was thirsty and had to pass water more frequently, while she began to lose flesh. Towards the end of February she began to have hysterical fits two or three times a day, and there was a vaginal discharge with much itching and irritation of the vulva. For this complaint she attended the out-patient department of the Women's Hospital. She always had a bad appetite till five weeks ago, since which time she had a constant desire to eat.

Present Condition.—Patient was a pale-faced brunette; she said she used to be quite stout, even up to Christmas. She weighed 6 stone 11¾ pounds. No jaundice, œdema, or cyanosis. Pulse 60; Temp. 98°; Resp. 24.

Alimentary System.—Many teeth were decayed, but she had not had toothache. Mouth dry; tongue dark red, clean, moist; hunger and thirst were constant. Had some pain in back, and occasional nausea after meals. Bowels confined for two days. Abdomen hard, retracted, and rather tender. Liver 4 inches in V. M. L. Spleen 1½ inch in M. A. L.

Circulatory System.—No palpitation or dyspnœa. Heart's impulse in 5th I. S. one inch internal to V. M. L. Area of dulness not increased. Sounds rather weak and prolonged. No murmur. Pulse 60, regular, tracing shows distinct evidence of increased tension, though the curve is small. (*See Fig.* 66.)

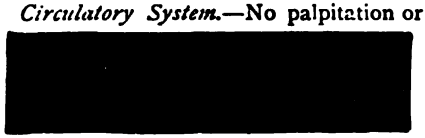

Fig. 65.

Respiratory System.—Normal.

Integumentary System.—There were a few patches of brown pigment on the abdomen near the umbilicus. No eczema.

Urinary System.—She had to rise three or four times at night to make water. Urine 106 oz., pale straw colour, acid, sp. gr. 1042; urea 1·1 per cent.; sugar 10 per cent.; no albumen; no blood. There was at times a faint haze of albumen, which was probably due to admixture with vaginal discharge, as it always coincided with the presence of leucocytes and squamous epithelium in the deposit. There was a marked ferric chloride reaction, but no acetone.

Vision.—Her eyes were carefully examined by Dr. Young, who found that vision corrected by glasses equalled ⅚ in each eye, and that there was no reduction of the field of vision or any ophthalmoscopic change. He reported that her inability to read was "purely due to weakened accommodation and a certain amount of retinal asthenopia arising from her weak state."

All the muscles of the eye may be affected by paralysis. Fienzal has related a case of sudden facial paralysis with corneal ulceration which ended in complete recovery. There was no history of syphilis or rheumatism, but the urine was loaded with sugar. *Keratitis* and *iritis* are not uncommon.

Diabetic Retinitis.—Diabetic retinitis was first described in

PLATE III.—Retinitis hæmorrhagica diabetica from a case of diabetes, aged 61.

1856 by Edward Jaeger, afterwards in 1858 by Desmarres, but until recently it has attracted little attention, the writers of special works contenting themselves with very brief references to it, while the general body of the profession is at most only aware that such a condition exists. This neglect has been no doubt due chiefly to the rarity of its occurrence; diabetes itself is one of the less common diseases, its average annual mortality being only two per 100,000 of the population, and the retinal changes occurring in only a small fraction of diabetics. But, in addition to this, an opinion prevailed formerly even among specialists that it was merely a variety of retinitis albuminurica. This was founded on the facts that the urine in most of the reported cases contained albumen as well as sugar, and that there is a general resemblance in the ophthalmoscopic appearances, though, as we shall see, more careful study has established well marked characteristic differences; while the cases recorded by Noyes, Desmarres, Eales, and others have proved that the presence of albuminuria is by no means constant.

Diabetic retinitis is invariably met with in elderly persons, and only in those in whom the disease has existed some time, although the derangement of the general health may have been so slight that diabetes has frequently been unsuspected, and has been first discovered by the appearances of the fundus leading to an examination of the urine.

Two well-marked varieties have been described (HIRSCHBERG):—

1. *Retinitis centralis punctata diabetica*, in which there is a characteristic inflammation of the central portion of the retina, causing small, bright spots arranged in groups, and often accompanied by hæmorrhages (*Plate III*).

2. *Retinitis hæmorrhagica diabetica*, in which retinal hæmorrhages occur, followed by inflammatory and degenerative changes (*Plate IV*).

3. Cases presenting the characters of both the above types or mixed forms are met with.

Retinitis centralis punctata diabetica, or central diabetic retinitis, is a truly characteristic affection. It occurs in persons of middle or advanced age who have been for some time the subjects of glycosuria, but its symptoms may be so slight that it is only discovered by an ophthalmoscopic examination. It is generally bilateral, but may supervene gradually or suddenly. The patients complain of dimness of sight, or of

a mist before the eyes, or of difficulty in reading, although they may preserve good vision for ordinary purposes. The external appearance of the eyes is perfectly normal, but visual acuity may sink to one-half or even one-twentieth of the normal, while there is a dark spot in the centre of the visual field (HIRSCHBERG).

The media of the eye are usually quite clear, although it is always possible that some opacity of the lens may be present, due to diabetic or senile changes, but not enough to account for the defect of vision. Serious cloudiness of the vitreous does not occur in this disorder. The chief causes of the visual disturbance are groups of small, clear, bright specks, situated in the structures of the retina in and around the central part, between the upper and lower divisions of the temporal branches of the retinal artery, also near the disc and on its nasal side.

As the spots in the centre of the retina grow larger, small streaks or crescents are formed, but they never assume the radiated appearance met with in retinitis albuminurica. There is never any pigmentation in or around the specks. Fine streaks and minute points or small spots of hæmorrhage occur around the bright spots, and occasionally in or upon them, and such hæmorrhages may be observed nearer the periphery than the white spots. Hæmorrhages are seen in all forms of retinal degeneration, but in this they appear never to exceed a certain size. Such small hæmorrhages may disappear by absorption, and new ones take their place; nor are the white spots quite permanent, though it is doubtful if they ever completely disappear. As a rule, they increase in size and number, and the visual disturbance, which may improve temporarily, remains stationary or gets worse. It is especially noteworthy that there is no affection of the optic nerve, and neither diffuse retinitis nor marked vascular change.

These characters suffice to differentiate it from any of the forms of albuminuric retinitis at the first glance. Nettleship thinks that the so-called white spots are also somewhat yellower than those seen in albuminuric retinitis; but this is not always the case. Leber, de Wecker, and Mackenzie believe that there is a much greater tendency to large hæmorrhages into the vitreous in diabetic than in albuminuric retinitis; and Nettleship has recorded a case in which the retinitis was complicated by the formation of blood vessels in the vitreous. "Over the whole of the central region," he

writes, "the retina is œdematous and hazy, in some parts densely cloudy. Near the yellow spot are some densely opaque yellowish-white clumps of deposit, such as have been described in other cases of diabetic retinitis. The retinal veins are considerably distended, and in various parts are a few scattered blood spots. Close to the *fovea centralis* two or three vessels of medium size suddenly appear in the retina; they cannot be followed to the optic disc, but have every appearance of springing from the choroid directly into the retina. The largest of them (seen at its apparent emergence from the choroid with + 2·5 D), followed upwards and outwards, is found to divide into a network of minute vessels, which project forwards in the form of fine loops into the vitreous, where the most prominent of them are seen with + 6 D. On a few of these loops an appearance of small swellings, perhaps capillary aneurisms, can be distinctly seen."

The following case was under the care of Mr. Eales, who sent her to me at the General Hospital.

CASE 49.—*Diabetes Mellitus—thirst—glycosuria—wasting—retinitis centralis punctata diabetica.*

Flora M., aged 49, married, was admitted into the General Hospital on Nov. 1st, 1892, complaining of thirst, pain in the left shoulder and in the chest, rising in the throat, inability to see clearly, everything looking like shadows, itching generally over the body, but chiefly in the palms of the hands and soles of the feet.

Family history.—Father dead, aged 61, paralysed; illness lasted a year. She says he suffered in some way from his water, but she was too young to know about it. Mother dead, aged 40, from "inflammation of brain" a month after the death of the father. There were five sisters and one half-sister, of whom three are dead, including the last; of three brothers one is dead, but patient knows of no case of diabetes or phthisis in the family. She has had eleven children, all of whom are delicate; her eldest son suffers from some chronic chest complaint, which he has been told is bronchitis.

Previous health.—Her general health has been fairly good, but she had croup several times when a child, and typhus (?) fever at the age of 14. She suffered much from flooding at her confinements, and was operated on ten years ago by Mr. Lawson Tait for a swelling in the right iliac region. A year ago she suffered from pain and throbbing on the top of her head, which, after poulticing, ended by a discharge of blood and matter down her nose! Last Easter she was ill for a month with vomiting and a burning pain in the stomach.

Her general surroundings at home have been very comfortable, her habits have been temperate, but she has been in the habit of drinking about a pint of beer daily.

History of present illness.—For three or more years patient has had to get up at night to make water, and for about the same time she has

suffered from thirst, but she thinks her sight has been failing for about five years.

State on Admission.—Patient is a sparely-nourished little woman, dark hair, sallow complexion, evidently a Jewess. No cyanosis, jaundice, or œdema. There is a linear scar in the middle line above the symphysis pubis. Height, 4ft. 9½in.; weight, 6st. 2lbs.; T., 97·4; P, 102; R., 18.

Alimentary system.—Appetite poor, mouth dry and parched, a good deal of thirst, throat dry, burning and rising in throat, weight and fulness after eating, pain at epigastrium going through to back, acidity and flatulence, also nausea at times, but no vomiting. Lips a good colour, teeth very deficient, tongue pale and slightly furred, stomach not dilated, bowels very constipated, there is a large prolapsus ani, liver dulness in V.M.L. 4¾ in., splenic dulness in M.A.L. 2¾ in.

Circulatory system.—Pain and palpitation in præcordia; she often feels faint. Form and appearance of præcordia normal, apex beat in 5th I. S. ½ in. internal to V.M.L. Heart's area of dulness not increased; sounds normal; pulse full, moderate tension.

Respiratory system.—No cough or expectoration. Chest expands well, but she complains of pain below the left breast, on taking a deep breath. Percussion note and breath and voice sounds normal; no friction.

Genito-Urinary System.—She has not menstruated for five years. Micturition is frequent, sometimes difficult, but never painful. The quantity of urine has varied, but never exceeded 64 oz.; sp. gr., 1029, acid, a faint haze of albumen (at times). Urea, 2·9 per cent.; sugar, 4·8 per cent.; no blood or bile; reaction with nitro-prusside of sodium and ammonia well marked, also with ferric chloride, but the patient is taking sodium salicylate.

Nervous system.—Patient complains of numbness and tingling in the palms of the hands and soles of the feet. Patellar reflexes absent; all other reflexes diminished. No loss of motion or sensation.

Ophthalmoscopic appearances in the right eye are as follow:—Optic nerve a little pale, edge quite distinct; in the outer quadrant of the retina large patches of a bright white colour, over the surface of which the retinal vessels can be traced; no hæmorrhages. Left eye: disc clearly defined; very similar white patches in the corresponding part of the retina with a punctiform hæmorrhage in one of them.

The pathology of the retinal affections of diabetes is undoubtedly the dyscrasia which gives rise to nutritive changes in the blood vessels and tissues of the body. The histological changes of this form have been very well worked out.

In a case recorded by Dr. Stephen Mackenzie the eyes were examined microscopically by Mr. Nettleship, who found the following changes:—

1. The *retina* was thickened in all its layers, the change being greatest in the nerve fibre layer, where there were numerous varicose swellings; the disc was slightly swollen and its nerve fibres converted into an intricate network of fine threads, the meshes being for the most part empty, but sometimes filled by swellings like those in the retina. The

ganglion cells and the granule layers were well preserved, and indeed more readily seen than usual, their elements having been, as it were, dissected apart by the effusion of fluid between them. The bacillar layer was wanting, and its place in some parts occupied by a layer of albuminous effusion. In the intergranule and molecular layers were round spaces filled with faintly refracting albuminous granules. The *membrana limitans interna* was much thickened in parts and thrown into abrupt folds, which, when deep, resembled papillæ. There were no distinct hæmorrhages in the retina, only one or two small patches of rusty granules near the disc.

2. The *vitreous* of the left eye contained a quantity of blood, the source of which could not be traced.

3. The *choroid* was unaltered at the margin of the disc, but was greatly thickened in other parts. This was due to great distension of the vessels, and to a collection of a faintly granular albuminous substance in the stroma between the vessels and in the elongated spaces of the *membrana supra-choroidea.*

4. The trabecular tissue of the *subvaginal lymph space* of the optic nerve was much increased in bulk by thickening of the individual strands and by increase in their number.

5. The *optic nerve* showed no very marked alterations, but its connective tissue nuclei were increased in number in and just behind the *lamina cribrosa.*

6. The *arteries*, especially the central artery and its branches, showed thickening of their coats, chiefly due to a deposit of hyaline material between the endothelium and the fenestrated membrane. In places, the thickening was fibrous. The whole vascular wall was swollen. The veins were, as a rule, merely distended. The capillaries were distended, and in the retina formed minute aneurisms, which usually contained reddish brown granules; their walls were not thickened.

In a case of Mr. Nettleship's, examined by Mr. Lawford, there was interstitial neuritis affecting the optic nerve, attributed to plugging of the central artery, which was present. The choroidal and retinal arteries showed hyaline thickening in places, with aneurismal dilatations and hæmorrhages. Large masses of "waxy" and granular material were observed in both granule layers, while others of smaller size could be seen in the nerve fibre layer.

The microscope therefore shows thickening and dilatation of the retinal vessels, capillary aneurisms, and a considerable

exudation of granular material between the two granule layers. It is probable that the condition is a true inflammation commencing around the vessels and attended by exudation of inflammatory products into the retinal substance, which presses upon and destroys the nervous tissues and finally undergoes fatty degeneration.

Hæmorrhagic diabetic retinitis, or the second type of this disease, differs from the preceding in the fact that the hæmorrhages constitute the essential part of the process as observed with the ophthalmoscope, and that any white patches which appear are merely due to inflammatory or degenerative changes in the damaged tissues and in the effused blood. It may, and not uncommonly does, begin in one eye. The hæmorrhages are usually punctiform, but occasionally striated, and are situated all over the retina, by no means being confined to the region of the disc. Their source is not the superficial retinal vessels, and their rounded shape indicates that they are situated below the nerve fibre layer. There may be some haziness of the retina pointing to some degree of œdema, and crystals of cholesterine may be visible in the vitreous. Nettleship has described a case in which "a venous branch of considerable size passing upwards from the main upper division of the *vena centralis* showed a number of small dilatations which gave the vessel an imperfectly beaded appearance."

CASE 50.—*Diabetes Mellitus—polyuria—wasting—pruritus vulvæ—heredity—phthisis—retinitis hæmorrhagica diabetica—acetonuria.*

Amelia M., fifty-seven, housewife, was admitted into the General Hospital on November 15th, 1889, complaining of weakness of sight, pain in the back, loss of strength, and irritation of the pudenda. Her symptoms had been coming on since the climacteric period, which commenced with her four years ago, though there was nothing more definite than weakness and wasting until the last six months. She had had no thirst, and polyuria had occurred only lately. The attacks of pudendal irritation had, however, troubled her from time to time for the past ten years, especially when pregnant.

Previous History.—She had enjoyed a comfortable home and good food, with half a pint of beer daily. She had had erysipelas twice, twenty-four and twelve years ago. She had small-pox at twelve years of age; could recollect no accidents or injuries. Had been married thirty-eight years, and had borne seventeen children besides five miscarriages. Ten of the children were alive and well; the others died young.

Family History.—Father died, aged sixty-four, of bronchitis; mother died, aged seventy-three, of "cancer of the face." One sister had died of phthisis and a brother of diabetes. Another sister died of fever in America. The others (eight) were alive and well. She knew of no cases

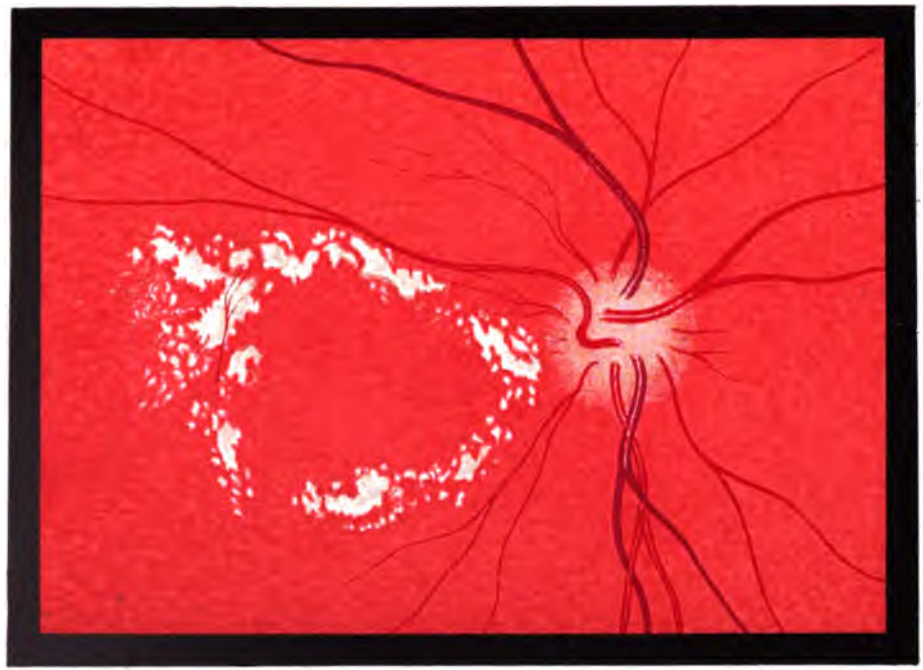

PLATE IV.—Retinitis centralis punctata diabetica from a case of diabetes, aged 63.

of gout, rheumatism, or insanity, and of no other cases of diabetes or phthisis.

State on Admission.—She was a well-developed stout woman, with a florid face, moist skin, and great varicose dilatation of the veins of the legs. No œdema. Temp. 98°, Pulse 96, Resp. 24.

Alimentary System.—Appetite poor; no thirst; no discomfort or pain after food. Teeth very defective; tongue clean. Bowels confined; liver dulness in V. M. L., 4½ inches: splenic dulness in M. A. L., 1 inch.

Circulatory System.—Area of cardiac dulness not increased. Heart's apex in fifth I. S. internal to V. M. L., sounds normal. Pulse 96, full, incompressible, regular.

Respiratory System.—Appearance of chest normal. Above right clavicle percussion resonance diminished, vocal resonance increased, expiration prolonged.

Ophthalmoscopic Appearances.—Right eye: Numerous punctiform hæmorrhages round disc, and many glistening white patches, varying in shape, and some of considerable size. Left eye: One small hæmorrhage on the inner side of disc, and in yellow spot region a large area of white glistening patches with numerous punctiform hæmorrhages.

Genito-urinary System.—Had not menstruated for three and a half years. There was no eczema about vulva; the pruritus had existed for three months. Urine 56 oz., sp. gr. 1035, acid, yellow, urea 1·8 per cent., a trace of albumen, sugar 6 per cent., acetone present.

Treatment.—House diet, no sugar; *Ext. Cascaræ Liq.* ℥x.; *Aquæ* ℥j.; thrice daily.

October 18th.—Diet: Meat, green vegetables, potatoes, one slice of toasted bread with each meal. Milk, two pints. Tea or coffee. The dose of fluid extract of cascara was increased to twenty minims.

October 29th.—Ordered, *Haust. Magn. Carb.;* thrice daily, and to be made an out-patient.

Her eyes were in the same state on her discharge. There had been no complaint of the pruritus during her stay in the hospital.

The following table shows the state of the urine during her stay in the hospital:—

DATE.	URINE.	SP. GR.	UREA.	SUGAR.
Nov. 17th	56	1035	1·8 p. c.	6 p. c.
,, 24th	46	1040	1·7 p. c.	6 p. c.
,, 26th	38	1040	—	5·8 p. c.

We are somewhat in the dark as to the actual anatomical changes in this condition, but the lesions are known to consist primarily of hæmorrhage, and secondarily of inflammation and fatty degeneration of the areas injured by the effused blood. I can find no account of any microscopical report on the eye in this type, but we may infer that there are degenerative changes in the arteries and capillaries very similar in

kind to those already described, and which are met with in many other parts of the bodies of diabetic persons.

The symptoms of the disease in both forms are due to failure of vision, which may be more or less sudden, and vary in amount. The patients often appear to complain of a mist or haze before their eyes, or of sparks, dark spots or muscæ, whilst in some cases disturbance of colour vision has been noticed. The course of the disease may be irregular, a succession of attacks of partially disturbed vision may occur, between which sight may be in a great measure restored (MACKENZIE). But in the course of time the lesions are progressive, and so far as we know they never end in recovery.

From the description already given, we learn that these appearances, when well marked, are fairly characteristic. They differ from the retinitis of Bright's disease not only in their general appearance, but in the following special points: —1. The patches are irregularly distributed around the centre of the retina, not specially near the macula, and are met with on the nasal as well as on the temporal side of the disc. 2. The patches are never arranged in a fan shape. 3. They are never associated with papillitis or diffuse retinitis. 4. The hæmorrhages are, as a rule, punctiform, and not striated. 5. Hæmorrhages into the vitreous are common. These lesions can hardly be confounded with syphilitic retinitis, which is a choroido-retinitis, is seldom free from pigmentary disturbance, and never presents the unpigmented white shining infiltration of the true retinal tissues seen in diabetes.

Hæmorrhages *per se* are of course not distinctive, but when hæmorrhage occurs into the vitreous we may lay it down as a rule that the urine should be examined for sugar.

The diagnostic significance of these changes, when well marked, is therefore very great; but it is never prudent to rely only upon the ophthalmoscopic changes when it is so easy to confirm the diagnosis by examining the urine for sugar.

The importance of the discovery of the occurrence of these changes for prognosis is undoubted, for there can be no question that they indicate advanced tissue degenerations and a more or less speedy break up of the constitution. In a case of otherwise mild diabetes with retinal changes I should form a very grave opinion of its future; and I have no hesitation in saying that such a view, though not supported by any statistical evidence, is based on sound pathological principles

Jaeger has recorded a case of diabetic *retinitis* where the swelling was so great as to hide the outlines of the disc, and was accompanied by numerous hæmorrhages and yellow patches. There was a marked central *scotoma.* Such central scotomata explain the occurrence of one form of diabetic amblyopia. There is loss of vision in the central part of the retina, just as in tobacco amblyopia; but cases have been observed in diabetics who were not tobacco smokers (GOWERS, JENSEN, NETTLESHIP and EDMUNDS), though they generally are. According to Samelsohn the scotoma may be sometimes peripheral.

Atrophy of the Optic Nerve may be caused by (1) effusion of blood within its sheath; (2) descending degeneration from brain lesions, or (3) ascending degeneration after destruction of the retina by hæmorrhages (SAMELSOHN); Nettleship and Edmunds have described a case in which the atrophy appeared to be primary, but the man was a large smoker of tobacco, so that it was not an uncomplicated case in its etiology.

SMELL AND TASTE.—Jordâo has recorded a case of blunting of taste and smell, but this may have been due to some cerebral complication.

EAR AFFECTIONS.—Deafness is generally due to inflammation of the middle ear, but it may be caused by œdematous swelling of the Eustachian tube (MIOT). Diabetic *otitis media* (GRIESINGER, JORDÂO, KÜLZ, RAYNAUD, TOYNBEE), has been described as an acute inflammation of the middle ear not dependent upon any external cause(?). The disease is characterised by intense pain localised in the mastoid region, and is accompanied by tinnitus and intense deafness. There is redness and swelling of the auditory canal with some mucopurulent secretion, and the tympanum is congested, swollen and dull. There is purulent inflammation of the mastoid cells. The disease comes on very suddenly, without any cold or coryza. The osseous tissue is extensively destroyed, and according to Raynaud the disease begins in the bone. Kirchner has described a case of double purulent otitis in a diabetic patient in which there was entire absence of fever.

These cases call for special local treatment on exactly the same principles as in non-diabetic cases, and although the prognosis is not favourable, they may heal very well.

In some cases deafness appears to be purely nervous in its origin, and may supervene at the same time as the commencement of the diabetes.

RESPIRATORY SYSTEM.—The late Warburton Begbie met with a case of *membranous inflammation* of the larynx and trachea in a male patient, aged thirty-nine, under treatment in the Royal Infirmary of Edinburgh for diabetes. The complication proved rapidly fatal, causing suffocation, but it was in all probability merely a case of diphtheritic inflammation occurring incidentally in a diabetic.

The lungs may be affected by *catarrh*, but the most common pulmonary trouble is *chronic pneumonic phthisis* with or without the presence of tubercle bacilli.* It comes on very insidiously, often with little cough or rise of temperature, and when discovered there is often a considerable area of lung invaded.

CASE 51.—*Diabetes Mellitus—phthisis—wasting—thirst—polyuria.*

Walter J. B., aged thirty-four, brass worker, was admitted into the General Hospital on July 16th, 1890, complaining of thirst and polyuria. His illness had existed for seven months.

Family History.—Father living and healthy. Mother died, aged thirty-three, of enteric fever. Had two brothers and one sister living, and in good health. There was no history of fits, cancer, diabetes, gout, rheumatism, or insanity in the family.

Previous History.—Patient had diphtheria when he was twenty-three years of age. He had never met with any injury.

Present Illness.—At Christmas, 1889, he found that he was passing an increased quantity of water of pale colour, which left a white deposit when it dried. He was also troubled with thirst, and noticed that he was losing flesh. There was also some irritation about the glans penis. He was under medical treatment for a week. Six weeks ago he began to suffer from cough and pain in his chest, and latterly he spat up some thick yellow phlegm, occasionally tinged with blood. There had been no night sweats. Appetite not increased. Bowels confined. At Christmas, 1889, he weighed 9 st. 10 lbs.

State on Admission.—He was a well-developed but spare man, weighing 7 st. 7 lbs. No jaundice or œdema. Temperature 97·8°; Respiration 28; Pulse 108.

Alimentary System.—Lips red and moist; teeth sound; tongue fissured, dry, and coated with yellow fur. Appetite good, but not excessive. No pain or nausea after food. Bowels very constipated. He complained of pain without tenderness across the abdomen below the umbilicus and round to the back. Liver dulness in V. M. L., 4 in.; splenic dulness in M. A. L., 1 in.

Circulatory System.—Apex beat in 5th I. S., internal to V. M. L. Heart not enlarged; sounds normal. Pulse regular and fairly strong.

Respiratory System.—He had a slight cough with scanty expectoration, containing numerous tubercle bacilli. There was flattening above and below both clavicles, and he complained of pain over the manubrium, which was increased by coughing or forced respiration. The percussion

* Out of five cases of diabetic phthisis recently under my care, in two no tubercle bacilli were found.

note was impaired at the right apex in the supraspinous fossa behind, and as far down as the second rib in front. The breath sounds were harsh, expiration was prolonged, accompanied by moist râles, and vocal resonance and vocal fremitus were increased.

Urinary System.—Urine 126 oz., pale straw-coloured, acid, sp. gr. 1031, urea 1·3 p.c., sugar 6·2 p.c.; no albumen.

In some instances *gangrene* of the lung takes place, from rapid sphacelus of parts affected by the inflammatory process.

CASE 52.—*Diabetes Mellitus—phthisis—gangrene of lung—death—autopsy.*

James B., twenty-nine, wire drawer, admitted June 27th, 1885, complaining of general weakness, wasting, and thirst.

History.—He had been ill eighteen months, the first symptom noticed being loss of weight. He used to weigh 13 st. His work was in an ill-ventilated shop, exposed to acid fumes; he drank about eight quarts of beer daily. His previous health had been very good. His father and mother and five of his brothers and sisters were dead, but he could furnish no precise information as to the causes of death. Three of his sisters were alive and well. Early symptoms of his illness were thirst and passing a very large quantity of water; his appetite had latterly been good, but he had got weaker. For a month past he had had a feeling of tightness of the chest and a cough. His eyesight had been unaffected.

Condition on Admission.—He was rather pale, hollow-cheeked and emaciated, weighed 9 st. His cough was frequent, expectoration about 1½ oz. daily, nummular, greenish grey. Chest flat and hollow below the clavicles. On the right side there was dulness at the right apex with bronchial breathing, metallic crepitations and whispered pectoriloquy; on the right side resonance at apex impaired, breathing harsh with a few crepitations. Pulse 108; Respiration 24; Temperature 101°; urine 298 oz., pale, clear; sp. gr. 1040; faintly acid; very faint cloud of albumen; 6·89 per cent. sugar; 0·7 per cent. urea; acetone reaction; ferric chloride reaction.

Progress of Case.—He was dieted and treated by extract of opium (gr. i.) thrice daily, and Vichy water. His urine fell to about 100 oz., sp. gr. 1031, sugar 5·8 per cent., but on July 15th, eighteen days after admission, at 9.40 p.m., he was found very weak, with quick pulse, laboured respiration and dilated pupils. He was conscious and lay quite quietly, but occasionally the right side of his mouth was drawn down by a spasmodic twitching of the platysma myoides. He died at 11 p.m., but he was still conscious shortly before the end.

The *post mortem* examination was made by Dr. Bull. The body was emaciated; there was no peculiar smell on opening the body, and the blood did not contain excess of fat. The left lung was free, œdematous and congested. No fluid in the pleura. Right lung adherent at upper part, which was converted into a large abscess cavity containing thick sanious fluid, which escaped on removing the lung. The inner surface of this cavity was rugged, dirty green, and a large piece of black gangrenous lung tissue hung by a shred from the posterior wall. Bands of tissue crossed the cavity. Its walls were very soft. It had no very offensive smell. The lower lobe was congested and œdematous, and

contained numerous patches of lobular pneumonia, some breaking down. The bronchial glands were greatly enlarged. There was no other special change noted in any other organ, except that the liver and kidneys were very large.

CIRCULATORY SYSTEM.—Valvular disease of the heart, as a consequence of endocarditis occurring in the course of diabetes has been described by Lecorché. According to his statement it usually affects the mitral, rarely the aortic valve. Maguire has met with one or two examples. It is undoubtedly very rare, as in my pathological experience I have only met with this complication once. Affections of the wall of the heart are common, of which the most serious are fatty and fibroid degeneration, which may be attended by attacks of angina pectoris (VERGELEY), but too often attract little attention until death occurs suddenly from syncope.

DIGESTIVE SYSTEM.—Affections of the gums are very common, the most frequent being a form of atrophy in which the teeth loosen and come out; but there is often more or less inflammation present, and the gums may be spongy and bleeding.

CASE 53.—*Diabetes Mellitus—thirst—polyuria—wasting—family history of diabetes—gingivitis—failure of strict diet to remove sugar—some improvement in general condition.*

Thomas C., aged thirty-six, engine-fitter, admitted to the General Hospital on July 16th, 1889, complaining of thirst, polyuria, weakness and wasting. He had been ill four months, his illness having begun with a slight cold and sore throat, for which he attended the hospital as an out-patient for two months without getting better, when he became very thirsty, his water increased to seven pints daily, he lost his appetite, his tongue was blistered, and his teeth grew loose. He lost weight very rapidly—seven pounds in one week—and had continued to waste ever since. He had been very weak in the legs lately, but the thirst and quantity of water had been less.

Family History.—Father died aged seventy. Mother died aged sixty, of bronchitis. One brother died of diabetes and phthisis. Was married, but wife died eighteen months before of inflammation of lungs. Three children alive and well. No history of gout in family.

Previous History.—Could remember no illness except occasional colds, and a crop of boils twelve years ago. Gonorrhœa eighteen years ago; no history of syphilis.

State on Admission.—Patient was a well-developed sparely nourished man; skin moist; face pale; lips a good colour. Temperature 98°; Pulse 58; Respiration 16. Weight 9 st. 5 lbs.; used to weigh 11 st. 2 lbs.

Alimentary System.—Teeth bad and loose, gums sore; tongue large, white, rather dry. Appetite fair; bowels confined. Liver dulness began in sixth interspace and extended two fingers breadth below the costal border. Splenic dulness normal.

Respiratory System.—No cough or pain in chest, but some dyspnœa on exertion. Percussion and auscultatory signs normal.

Circulatory System.—No palpitation or pain; heart's area not enlarged; apex beat in 5th I. S. inside V. M. L.; sounds normal. Pulse regular, not easily compressible.

Nervous System.—Knee jerks present. Special senses normal. No neuralgic pains or abnormal sensations. Complained of feeling very *irritable* since illness began.

Genito-urinary System.—Total loss of sexual desire. Urine 92 oz.; sp. gr. 1040, acid, pale amber; urea 1·5 per cent., a very faint haze of albumen; sugar 7·4 per cent.; under microscope only bacteria visible.

Treatment.—Diet: Mutton, beef jelly, milk two pints, Vichy water (Haute Rive) and lemon juice. He had no medicine except an occasional aperient. His stay in hospital was only troubled by toothache, which occurred on July 22nd, and lasted some days. He was made an out-patient on September 12th, having been in hospital about two months.

The following table shows the result of treatment.

Date.	Urine.	Sp. gr.	Urea.	Sugar.	Wt. of Patient.
July 17th...	92 oz.	1040	1·5 p.c.	7·4 p.c.	9 st. 5 lbs.
„ 23rd...	96 oz.	1035	2·8 p.c.	6·2 p.c.	8 st. 13 lbs.
„ 30th ..	68 oz.	1037	2·8 p.c.	4·6 p.c.	8 st. 12½ lbs.
Aug. 6th...	90 oz.	1037	—	4·8 p.c.	9 st. 0 lbs.
„ 14th...	100 oz.	1032	2·2 p.c.	3·6 p.c.	9 st. 2 lbs.
„ 19th...	80 oz.	1030	2·4 p.c.	2·6 p.c.	— —
„ 22nd...	96 oz.	1036	2·8 p.c.	5·4 p.c.	9 st. 2 lbs.
„ 25th...	106 oz.	1036	—	4·6 p.c.	— —
„ 29th...	96 oz.	1036	2·0 p.c.	5·1 p.c.	— —
Sept. 1st...	90 oz.	1037	—	5·7 p.c.	— —
„ 5th...	96 oz.	1040	1·8 p.c.	5·4 p.c.	— —
„ 8th...	98 oz.	1039	2·5 p.c.	5·4 p.c.	— —
„ 11th...	106 oz.	1036	2·1 p.c.	4·0 p.c.	9 st. 9¾ lbs

After becoming an out-patient he continued to gain weight, until he reached 10 stone. He passed about five pints of water daily. In Dec. he complained of profuse sweating. He was treated with various drugs—opium, cocaine, and phosphorus—without any very definite effect; but on the whole he had made progress up to the time he was last seen (April 29th, 1890).

The *mouth* is generally dry, but salivation may be profuse (ROLLO). Occasionally complaint is made of hot sour risings into the mouth, causing the teeth to feel as if they were set on edge (ROLLO). Pavy has described a sense of emptiness at the pit of the stomach. Rosenstein states that the gastric juice often contains no free hydrochloric acid, which may be due to nervous causes, but where permanent is the result of atrophy of the glands from interstitial gastritis. Gans has

examined the stomach in eleven cases of diabetes and found the digestive capacity and mobility of the stomach always normal. On the other hand Honigmann found out of seven cases free hydrochloric acid absent in three. In my cases I have observed absence of free hydrochloric acid, with no deficient digestive action in the filtered gastric contents or loss of motor power, but I have not examined many cases. Heller has stated that the gastric juice contains sugar, but Ponomaroff denies this. *Ulceration* of the stomach and intestines may occur, giving rise to vomiting and diarrhœa. The bowels are generally constipated, but *diarrhœa* is sometimes present, generally depending on catarrh.

CASE 54.—*Diabetes Mellitus—rheumatic pains—polyuria—thirst—emaciation—improvement on diet and opium—diarrhœa—failure of jambol.*

Mary P., aged fifty-three, attended as an out-patient on May 4th, 1886, complaining of pains in the back and legs, thirst, loss of flesh, and of passing a great quantity of water. She had been ill four years. The quantity of water in twenty-four hours was about nine pints, sp. gr. 1030, loaded with sugar. She was treated by anti-diabetic diet, extract of opium (gr. i.) three times daily, and allowed saccharin as a sweetening agent. On this treatment the quantity of urine fell rapidly to four pints in twenty-four hours, and thirst was lessened. The following year she began to suffer from repeated diarrhœa. Jambol was tried as a substitute for opium, with some temporary rise in the quantity of water. The diarrhœa had to be kept in check by the use of chalk and opium; the urine remained about the same, four pints, sp. gr. 1039, when last seen in Sept. 1887.

Edwards has related the case of a child, aged seven, who after suffering from symptoms of diabetes for three or four months, was seized suddenly with pain and tenderness over the abdomen. Examination showed a considerable quantity of ascitic effusion. The temperature was 102°. His diagnosis was *acute peritonitis* with effusion. Death occurred the same night, but no autopsy appears to have been made.

Hirschfeld has described a type of diabetes in which assimilation of albumen and fats is deficient; it is characterised by early attacks of colic which do not occur later, by absence of polyuria, and sometimes by whitish fæces though no lumps of fat are visible. He suggests the very probable explanation that the colic is pancreatic, and that the disease is due to calculi in the pancreatic duct setting up atrophy of the gland.

Jaundice may occur as an accidental complication, and on its supervention the sugar as a rule disappears from the urine,

but this is not always the case, as shown in Case 28 (page 231).

Cirrhosis of the liver is more of a pathological than a clinical complication, but enlargement of this organ can be not uncommonly detected on physical examination, and is due to a process of interstitial inflammation which in a certain number of cases leads to atrophy. In some cases, as already mentioned, the cirrhosis is of a peculiar character, and gives rise to the type called by Hanot *diabète bronzé*, of which the following case is an example:—

CASE 55.—*Bronzed Diabetes—glycosuria—polyuria—thirst—wasting—enlarged liver—pigmentation of skin.*

Henry S., ætat 47, admitted March 6th, 1891, complaining of thirst and loss of flesh. He had been ill only two mon hs.

Family History.—Father died of consumption at the age of 36; mother died aged 77, but he cannot say from what cause. Two brothers are said to "suffer from their livers," one is in America, the other at home, both have dark complexions and have got darker of late years. Three sisters are alive and in good health; they are not particularly dark skinned.

Personal History.—Patient is married, the father of six healthy children: in addition, his wife has had six miscarriages. He has a comfortable home and surroundings. He is by trade a glass cutter, and he worked at it up to the age of thirty-two, when he took a public house which he held for eleven years; then he tried to resume his trade but found that his eyesight had become weak, so that he became a grocer's shopman. He has enjoyed very good general health until recently; he has never met with any serious injury; there is a doubtful history of syphilis in youth, *viz.*, a sore not followed by any constitutional symptoms; six years ago he had typhoid fever: he denies having been intemperate, but admits that he had been taking a little spirits every day.

Present Illness.—About six weeks ago he noticed there was a dull aching pain in the lower part of his back, his friends told him he looked thinner, his thirst became insatiable, and his urine was pale and abundant.

State on Admission.—Patient is a well developed, sparely nourished man, 5-ft. 8-in. in height, weight 10-st. 4-lbs.; he was 11-st. a few weeks ago. His complexion is a very dark olive; but the skin becomes abruptly paler near the root of the hair; the rest of the body is not so dark as the face; the conjunctivæ are very dark and injected. He says that he has been getting darker since he was about thirty years of age. Temp. 37·6°, Pulse 54, Resp. 20. His lips and gums are dark in colour, and the latter bleed easily: his teeth are worn down evenly (gouty?) but fairly sound. Tongue dry and furred in centre. Bad taste in mouth in morning; appetite good; no discomfort after meals, nausea or vomiting; bowels confined. There is tenderness on palpation below the costal margin and the edge of the liver can be felt below the ribs. The liver dulness in the vertical mammillary line is 5 inches; splenic dulness 1½ inch. The circulating and respiratory systems are normal. He complains of pain before passing water, and of too frequent micturition; he has to get

up two or three times in the night. Quantity 140 oz., sp. gr. 1036, pale straw colour, acid, a very faint haze of albumen, sugar 8 per cent., urea 0·7 per cent., acetone present, no ferric chloride reaction. Later in the case this reaction was constant. His blood showed corpuscles 91 per cent.; hæmoglobin 60 per cent. On his attention being drawn to his liver he told us that ten years ago his doctor had treated him for "enlarged liver," but he could not say whether he was cured. He was discharged on April 18th, unrelieved.

Marie has written a very good account of this condition, which he prefers to regard as a distinct morbid entity apart from diabetes.

ENTERIC FEVER.—There seems to be a more than ordinary liability in diabetics to suffer from enteric fever. Numerous cases have been recorded by Rayer, Griesinger, Bamberger, Gerhardt, Ryba and Plumert, Seifert, Ebstein, etc. The sugar may disappear during the course of the fever. The prognosis is said by Ebstein to be unfavourable. Bernard noted the absence of glycogen from the livers of fever patients. Noel Paton says that in animals diminished heat elimination increases glycogenesis, but in fever processes due to the growth of micro-organisms, this function is diminished.

CASE 56.—*Diabetes Mellitus—polyuria—thirst—wasting—intercurrent pyrexia resembling typhoid.*

Agnes L., eight, school girl, was admitted into hospital on February 7th, 1887, complaining of thirst, hunger, headache, and passing a large quantity of water.

History.—Her mother had noticed that these symptoms had been coming on for six months, as she was constantly drinking water and losing flesh. She had been previously pretty well, but never strong since she was four years old. Her sister was with her in the hospital with diabetes, and another child had died of the same disease at the age of eleven. Six others and the father and mother were alive and well. Nothing was known of any other cases of diabetes in the family.

Condition on Admission.—She was a small, ill-nourished child, of strumous appearance. Temp. 98°, Pulse 96, Resp. 18. Her tongue was dry and clean; the only abnormal signs were deficient resonance and feeble breath sounds at the left apex. Urine 58 oz., sp. gr. 1013, acid, contained 3 per cent. of sugar; no albumen.

Progress of Case.—She was dieted and treated by alkalies and cod liver oil. On this treatment the urine increased in amount, but the sugar diminished and was often absent. She gained weight; but in the middle of February she complained of her throat being sore, and though there was nothing to be seen, her temperature for five days was 101° each evening. During this time the urine fell from 80, 90, or even 130 oz. to 30, 40, or 50 oz. daily, sometimes containing no sugar.

The temperature was normal on the 18th and 19th; on the 20th it rose to 100°; was normal on the 21st; then began to rise, and for the next

fifteen days described a course very like that of a typhoid relapse (*Fig.* 67). She complained of abdominal pain, her tongue was dry and coated, her face flushed, and the spleen was distinctly enlarged.

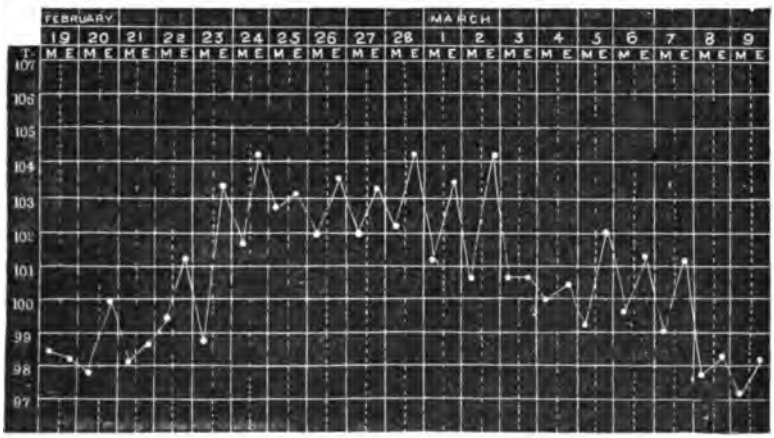

Fig. 67.

On the 28th February, and 1st, 2nd and 3rd March, some very suspicious looking spots were seen on the abdomen, and on one day she passed what was said to be quite a typical typhoid stool; but no other spots came out, and on the 8th the temperature was normal. During the period of fever the urine was never more than 44 oz. daily, and sometimes under 20 oz., while there was often no sugar present, and never more than 0·7 per cent.

After this she went on fairly well, but it was difficult to feed her. On her discharge she was improved in appearance, and had gained 6 lbs. in weight.

RHEUMATISM. — Rheumatic muscular pains are very common in diabetes. A patient who was taking 1½ oz. of dilute lactic acid daily, complained of profuse sweating and pain, but there was no rise of temperature nor any swelling of the joints.

CASE 57.—*Diabetes Mellitus—thirst—polyuria—rheumatic pains—night sweats.*

John B., aged fifty-five, wire drawer, was admitted into the General Hospital on September 19th, 1889, complaining of polyuria, wasting, and pain in the morning in the left shoulder. About sixteen months ago he began to complain of pains which he attributed to rheumatism, and his water was greatly increased, the necessity to pass it causing him to rise five or six times in the night. He was very thirsty and drank about a gallon of water or beer daily. A few months later he began to sweat very badly at night.

Previous History.—He had never been very well, and for the last twenty years had suffered from winter cough.

Family History.—Father died aged sixty-eight. Mother died aged sixty, after a paralytic stroke. One brother died of pleurisy; two were living, one of whom suffered from rheumatism and sciatica. A sister died from tumour of the breast, which was removed; two others were living in fair health. He did not know of any case of diabetes or phthisis in the family.

State on Admission—He was a slenderly-developed, sparely nourished man, with pale cheeks and lips; skin normal, moist; he said it used to itch badly in the early part of his illness, and that three or four of his fingers gathered, but he had had no eruption. Temp. 98°; Pulse, 84; Resp. 14. Weighed 6 stone 12 lbs., and six months before weighed 7 stone

Alimentary System.—Teeth fairly good, had been loose at times, and occasionally ached; they were much discoloured. Tongue large, covered on dorsum with a moist white paste. Thirst and appetite varied; sometimes they were marked. No pain after food. Bowels regular. Liver dulness in V.M.L. 4½ inches. Splenic dulness in M.A.L. 2½ inches.

Respiratory System.—No cough, pain, or dyspnœa. Percussion note resonant. Breath sounds normal.

Circulatory System.—No pain, palpitation, or dyspnœa. Area of cardiac dulness not altered. Apex beat in 5th I.S. in V.M.L. Sounds normal; pulse regular, full; artery rather hard.

Nervous System.—Eyesight very bad; ophthalmoscopic appearances normal: marked hypermetropia.

Urinary System.—Urine 116 oz., 1035, acid, pale limpid, urea 0·7 per cent.; no albumen; sugar 6 per cent.

Treatment.—Diet: House diet, green vegetables, Vichy water and lemon juice.

Sept. 20th. Ordered *Ext. Opii*, gr. j., three times daily.

Oct. 4th. He was put on a course of *Liq. Arsenicalis*, beginning with 5 minims thrice daily, the dose to be increased 1 minim each day.

Oct. 17th.—He was made an out-patient.

The following table shows the progress made.

DATE.	URINE.	SP. GR.	UREA.	SUGAR.	WT. OF PATIENT.
September 19th	138	1035	1·1 p. c.	6·4 p. c.	— —
„ 22nd	84	1035	1·5 p. c.	5·7 p. c.	— —
„ 25th	139	1031	0·8 p. c.	4·8 p. c.	7 st. 2 lbs.
October 2nd	118	1031	2·3 p. c.	3·7 p. c.	— —
„ 6th	130	1035	2.3 p. c.	5·2 p. c.	7 st. 1 lb.
„ 10th	98	1040	1·9 p. c.	4·8 p. c.	— —
„ 13th	126	1035	1·1 p. c.	4·4 p. c.	— —
„ 16th	114	1034	1·6 p. c.	4·8 p. c.	7 st. 5 lbs.

During the last fortnight of his stay in hospital his urine gave the reaction of acetone, but this did not have any consequences. He has since been kept under observation as an out-patient, and treated with cocaine, phosphorus, and salicylate of soda, without any decided benefit. On

March 25th, 1890, he weighed 6 stone 9 lbs., having recently lost weight, and on careful examination it was found that his liver dulness measured 5½ inches in the V.M.L., passing 3 inches below the costal border.

Thickening and shortening of the palmar aponeurosis (Dupuytren's contraction) have been several times recorded (CAYALA, BORDIER).

NEW GROWTHS. According to some authorities diabetic patients are specially liable to the formation of tumours, but they are of relatively slow growth (TUFFIER).

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CHAPTER XX.

DIABETIC COMA.

PROUT wrote that diabetics may be considered as existing on the brink of a precipice, and since Prout s time the very precarious tenure by which they hold their lives has come tc be very generally recognised. We are all aware of the great risks to which they expose themselves in travelling, probably on account of the unavoidable annoyances, as well as fatigue, which travellers even in these days must put up with. Violent mental emotions and bodily fatigue are well known dangers which we cannot be too careful to warn our diabetic patients to avoid.

It is understood that diabetics are more liable than other persons to the usual sort of accidents that befall any one occasionally : thus a diabetic is more likely to have an attack of pleurisy or pneumonia, and such inflammations not unfrequently pass on to breaking down of the lung, or even to gangrene of the inflamed part. But besides this special predisposition to inflammatory diseases, there is a complication of diabetes which has something characteristic and peculiar in it, so that of late years it has received a good deal of attention from some of the best clinical observers. It differs from those already alluded to by the alarming rapidity with which death may supervene in the midst of apparent good health. This it is to which the name of Diabetic Coma has been given, from coma being the final and most constant phenomenon.

As is well known, diabetic coma was described by Küssmaul, in 1874. His paper did not meet with the attention it deserved, in this country, until public interest in the subject was aroused by Sir W. Foster's graphic description of two cases which had come under his observation, in a paper read at the Manchester meeting of the British Medical Association, in 1877. Since that time, many other cases have been recorded, and the general clinical history of the condition has been elaborated by many writers.

ETIOLOGY.—The frequency with which deaths from this cause occur, may be inferred from the statement of Mackenzie, that of the instances of fatal diabetes collected by him from the registers of the London Hospital, all those under the age of twenty-five, with only one exception, had died of coma.

The statistics of Guy's and the London Hospital, show very clearly the greater frequency of this mode of termination of diabetes in young persons, so that *youth* appears to be a predisposing cause. *Sex* has no special influence that has been yet made out, nor does such an influence seem probable. *Condition of life* also appears unimportant.

Constipation has been a marked feature. It occurs most commonly in *acute* cases, and, as proved by the *post mortem* examination of the intestines, has existed to a far greater extent than had been suspected during life, so that I rate it highly in the list of predisposing causes. That the intestines are the seat of numerous fermentative and putrefactive processes is now well known, and it is easy to understand that constipation acts unfavourably in two ways: (1), by diminishing elimination of effete matter by one of its ordinary and most important channels, and (2), by affording time for the development of fermentative processes giving rise to the formation of toxic substances which may be absorbed into the blood.

It is only too true that the life of a diabetic hangs by a thread, and we cannot be too careful or too persistent in our warnings. Above all we should not allow cases of advanced diabetes to travel; too many of those who go to foreign health resorts in the hope of finding a cure, die of coma very soon after their arrival. This fact was insisted on by Prout, and is well illustrated by examples related by the physicians at the French and German spas frequented by diabetics. Clinical experience has suggested the dangers of *muscular fatigue*, *nervous shock*, and *exposure to cold*.

Bond and Windle in their remarks on a fatal case of diabetic coma which occurred at the General Hospital, say that the change from ordinary diet to richly albuminous food has been present as a factor in this and one other case under their observation. While not doubting the influence which great and sudden changes in diet can produce in the system, it is noteworthy that in the case published by my colleague, Dr. Rickards, the patient was taking ordinary diet.

PATHOLOGY.—Our knowledge of the pathology of this subject has been much widened, and our view of it has gained much in comprehensiveness from the writings of Senator, who has sought to establish the existence of a self-infective process, dependent upon the formation of toxic substances in normal or pathological cavities of the body, which, occurring in many other conditions besides diabetes, gives rise to phenomena essentially identical with those described by Küssmaul. He has recorded seven such cases; two of chronic cystitis, two of gastric cancer, and three of pernicious anæmia. In none did the urine contain any sugar, or give a reaction with ferric chloride. Riess has described eight cases in anæmia, five in anæmia with renal disease, and four in gastric and hepatic cancer. Von Jaksch has published a case of "coma carcinomatosum," in a patient the subject of gastric cancer, the urine containing acetone and aceto-acetic acid but no sugar. Litten has described one case which occurred under what he calls "dyspeptic conditions," and which terminated in recovery, but the patient was a boy convalescing from scarlatina, and suffering at the time from albuminuria.

I am, therefore, disposed to accept the view that Küssmaul's coma, if I may be permitted to use this convenient term, is not restricted in its occurrence to cases of diabetes, but may be met with in several other diseases, especially in those in which the state of the blood has undergone profound pathological alteration.

This is proved by the case of Harriet B., which is published at length at page 62. In that case, the cause of the coma was pyonephrosis with renal calculus, and there was no glycosuria, but the type of coma corresponded to Küssmaul's description.

Various theories have been brought forward to account for the symptoms. As is well known, Küssmaul adopted the view that the phenomena depended upon poisoning of the nerve centres by acetone.

Acetonæmia was not altogether a new idea in pathology, as Petters, as long ago as 1857, had found acetone in the blood, expired air, and urine, of a severe case of diabetes. Later on Kaulich noticed an acetone-like smell in the urine of patients suffering from variola, typhus, and pneumonia. The presence of acetone in diabetic urine was subsequently confirmed by Cantani, Kaulich, Rupstein, and Fleischer. There is very little doubt that acetone is frequently present in the urine of

diabetics, but it is met with in many other diseases; thus Bull, who investigated this point at my request, found it present in five out of twenty-one cases of pneumonia, in acute chorea, intestinal colic, tonsillitis, fractures, burns, and contusions.

The blood of Sarah L. (Case 60) was distilled very carefully, but no acetone could be detected in the distillate. These investigations were conducted in Prof. Tilden's laboratory, where I had the great advantage of his kind assistance and co-operation. Moreover, Dr. MacMunn could find none in the blood of F. R. W. (Case 58).

Another difficulty in the way of accepting the view that acetonæmia is the cause of these toxic symptoms, is that it has not been proved that acetone is capable of giving rise to similar physiological effects. Küssmaul obtained results which were of a not very decided character, but more recently Salomon and Brieger have shown that acetone in large doses produces no effect on animals or men, even when diabetic. The urine of the subjects of these experiments had no smell of acetone, gave no reaction with ferric chloride, nor any of the chemical reactions of acetone, so that it must have been destroyed in the body

Similar experiments by the same observers with aceto-acetic acid, caused acetone to appear in the urine, where it announced its presence by its smell, the iodoform reaction, and its characteristic combination with bisulphide of soda, but in no case did the urine give the ferric chloride reaction.

Very large doses were without any noticeable effect; neither dyspnœa nor somnolence was produced; after the doses had been continued for many days, there was some loss of appetite, and the breath acquired a peculiar aromatic smell.

Penzoldt has stated that when excretion through the lungs is retarded, the introduction of large quantities of acetone into the circulation of rabbits, is followed by intoxication, hebetude, and coma, and he contends that when the lungs are disabled from any cause, these results will follow acetonæmia in man. Unfortunately for the application of these facts to the explanation of the cases under consideration, the absence of pulmonary complications has been specially noted in the majority of them, and has even formed the basis for an aphorism, viz., "that when pulmonary disease is absent or

slight, the occurrence of coma is more to be feared, especially the younger the patient and the more acute the disease." (MACKENZIE.)

Senator in the paper already alluded to suggests that *trimethylamine* may be the toxic agent, but advances little evidence in favour of this hypothesis.

Minkowski has discovered the presence in the blood of diabetics of large quantities of an acid, which he believes he has identified as *β-oxybutyric acid*, one of the isomeric series of butyric acids, and has introduced a new theory by calling attention to the toxic influence of large quantities of acids when introduced into the body. Von Noorden believes that this acid is the essential cause of the coma. He points out that its presence may be inferred when the urine is dextrotatory after the glucose has been removed by titration with Fehling, or precipitation by basic acetate of lead and ammonia.

Walter, in the course of some researches into the effects of *acids* on the animal organism, noticed that in rabbits the introduction into the stomach of large quantities of diluted phosphoric and hydrochloric acids was followed by "dyspnœa, depression of the heart's action, and death by collapse." *Post mortem* examination showed in some cases erosion of the mucous membrane of the stomach, and the coagulation of the blood was delayed. The objection that the symptoms might have been due to the local action of the acids on the stomach, was disproved by the effects of *subcutaneous* injections of alkalies, which prevented or cut them short. From his investigation, he arrived at the conclusion that the dealkalisation of the blood by the introduction into the body of excess of acids, causes first stimulation, and later on paralysis of the respiratory centre.

It is important to notice that β-oxybutyric acid is capable of breaking up to form di-acetic acid, which yields on decomposition acetone and carbonic acid, so that this substance must be regarded as being nearly allied to acetone.

Binz has found that sodium butyrate produces coma in cats.

Latham has suggested the following theoretical explanation of the production of a toxic substance in the blood. He thinks that the second cyan-alcohol $C_2H_4 \left\{ \begin{matrix} OH \\ CN \end{matrix} \right.$ is converted by hydration into lactic acid, which if not completely

oxidised into CO_2 and H_2O would first form aldehyde, thus :—

$$C_2H_4\begin{cases}OH\\COOH\end{cases} + O = \begin{cases}CH_3\\COH\end{cases} + CO_2 + H_2O.$$

Lactic Acid. Acetic Aldehyde.

Then by condensation :—

$$3\,C_2H_4O = C_6H_{12}O_3$$

Paraldehyde.

This is a hypnotic, and would cause drowsiness.

Or he suggests that the third cyan-alcohol $C_3H_6\begin{cases}OH\\CN\end{cases}$ might be hydrated into oxybutyric acid.

In spite of the negative results of most *post mortem* examinations, an attempt was made by Sanders and Hamilton to find a structural basis for these symptoms. Their view, as is well known, was that the respiratory and nervous phenomena are caused by fat embolism of the pulmonary and cerebral capillaries. They based this theory on the results of the *post mortem* examination of one case of diabetic coma, in which the blood was very fatty, and fat embola were found in the lungs and kidneys.

It is curious that Küssmaul's first case had also fatty blood, and the lungs presented numerous small infarcts respecting which he remarks, "perhaps we might attribute to the lipæmia and fat embolism the numerous small lung infarcts, at least another source of embolism was not to be discovered *In no case could the fearful terminal dyspnœa have originated in these small infarcts, the greater part of which were of far older date.*" Thus this theory had not escaped the notice of Küssmaul, although he merely noticed it to dismiss it. Lipæmia is only exceptionally present in diabetic coma, and even when it exists, fat embolism may not occur (TAYLOR, DRESCHFELD); in two cases with lipæmia, examined by Mr. Barling and myself, the fat in the vessels had assumed rather the appearance of *post mortem* thrombi than of embolism, and was less than we found in many cases of fracture where it had given rise to no symptoms at all during life.

Although Stockvis and even Ebstein, maintain the uræmic origin of the coma, they have found few supporters; clinically, it differs from the classical type of uræmia, in which convulsions play the leading *rôle*; etiologically, neither albuminuria nor suppression of urine nor diminution in the normal urinary solids is a constant phenomenon; finally, the doctrine

of uræmia rests on quite as uncertain a basis as that of acetonæmia.

In concluding this part of the subject, I may express my own opinion, that, while at present we are unab e to determine positively the nature of the toxic substance, or the determining causes of the sudden explosion of the fatal terminal symptoms, these phenomena are toxæmic, and in diabetes depend upon the presence in the blood of some substance nearly allied to acetone.

There has never been any dispute that *heart failure* is the obvious explanation of a certain number of cases of sudden death in diabetes. This is said by Schmitz to be due to *fatty degeneration* of the heart, which is a common form of cardiac degeneration in diabetes. Frerichs has suggested that the muscular fibres of the heart undergo a "glycogenic degeneration," in which their power of contractility is lost, but it is doubtful if the deposit of glycogen injures the heart's muscle.

SYMPTOMS.—The premonitory symptoms vary very much. Sometimes the attacks begin with maniacal excitement; more commonly abdominal pain or headache is complained of; a sudden fall in the sp. gr. and sugar contents of the urine has been sometimes noticed, but this is by no means always a cause for alarm.

Lépine attaches much importance to the rapidity of the pulse as a trustworthy prodromal sign.

The urine usually gives a Burgundy red colour on the addition of a solution of the perchloride of iron, the colour disappearing on heating the mixture. This reaction is certainly present in diabetic urine apart from coma, and has been met with in other diseases. Thus Von Jaksch has met with it in many acute disorders, especially measles, scarlatina, and pneumonia. He has also observed it in a case of gastric cancer terminating fatally by coma. Hoppe-Seyler has described it in a case of sulphuric acid poisoning as occurring during the time no food was taken. Senator observed it in a case of atropine poisoning which died comatose. Windle has observed it in pneumonia, Bright's disease, scarlatina, and several other pathological conditions apart from diabetes. It cannot be therefore regarded as in any sense a pathognomonic sign, and it was absent in Case 65.

Acetone is present in the urine, as indicated by a rose-violet coloration with a solution of nitro-prusside of sodium and ammonia. So far as I am aware, this is constant; the

amount present varies greatly, but it may be due to the diet, and disappear when carbo-hydrates are allowed (HIRSCHFELD). A trace of *albumen* is very commonly to be found.

Another symptom which is very striking, but not always present, is the peculiar odour of the breath, which has been variously described as like sour beer, apples, hay, chloroform, and acetone.

The patient gradually becomes more drowsy, the respiration acquires a deep sighing character, the surface of the body grows cold, the pulse is weak and rapid, complete unconsciousness supervenes, and in this state he may remain several hours; death is sometimes preceded by convulsions; the temperature is usually subnormal, but in rare cases is raised.

Frerichs attempted to give greater precision to our study, by classifying cases of sudden death in diabetes into three groups.

In the first group he placed those which suddenly, and usually after previous exertion, become prostrated, with cold extremities, small failing pulse, drowsiness, and loss of consciousness, and terminate fatally in a few hours; these he called death from heart failure.

In the second group the duration is longer, and there is a prodromal stage which may be either general prostration, gastric disturbance, vertigo, vomiting, constipation, or a local disease, such as a dental abscess, pharyngitis, an abscess with a tendency to gangrene, bronchitis, or catarrhal pneumonia. The attack itself commences with headache, restlessness, delirium, anxiety, sometimes with maniacal outbursts, dyspnœa, characterized by frequent deep respiration with free entrance of air into the lungs, sometimes with cyanosis, sometimes without it, feeble rapid pulse, low temperature, drowsiness and coma. The breath has a peculiar smell like fruit or chloroform, or acetone. Such cases may recover temporarily, and in some rare instances the attack may pass away. The duration of the symptoms may be from twenty-four hours to three or four days, or even longer. He attributed this type to a peculiar unknown poison, perhaps acetone, acting on the respiratory centre.

In the third group he placed cases which present no dyspnœa or anxiety, have moderately firm pulses, and are fairly well nourished. The attack is characterised by headache, a feeling of intoxication, disordered gait, sleepiness, and gradual coma,

from which they do not awaken. The breath has the characteristic smell. This was believed by Frerichs to be the consequence of a poison which affected the nervous system like alcohol.

In the first group the symptoms are those of collapse, coma occurring only at the end, and the duration of the whole attack is very short. In the second group we have Küssmaul's typical complex of symptoms, with dyspnœa, peculiar odour of breath, and coma. In the third group there is no dyspnœa, the symptoms more closely resemble alcoholic intoxication, but the breath has the characteristic smell, and coma is present. I cannot recall a case of mine in which deep breathing, or the so-called dyspnœa, was not present, but examples have been recorded (FRERICHS, PRESCOTT ROBERTS).

The following cases illustrate the usual pathological and clinical features of diabetic coma as I have observed it:—

CASE. 58.—*Diabetic coma—death—autopsy.*

F. R. W., an engine driver, aged forty-one, unmarried, was admitted on May 17th, 1884; he had been attending as an out-patient since the previous December.

His own account of himself was that he had always been a healthy man; he came of a good stock, his mother and several brothers and sisters being alive and well, and his father having died of smallpox at the age of fifty-four. About a month before he was first seen, he was leaning over the strap of the fly-wheel, cleaning his engine, when his foot slipped, and he fell so as to contuse his abdomen and strain his back. He came at once to the hospital, and was treated surgically for the strain, but got weaker, and was eventually transferred to my care.

At that time he had lost a good deal of flesh, he complained much of weakness, and passed a large quantity of water, which was loaded with sugar, but contained no albumen, and gave no special colour reaction with ferric chloride. On modified diet and treatment he improved somewhat: that is to say, the quantity and sp. gr. of the urine were reduced; but he continued to lose weight, and became so very anæmic and weak, in spite of iron and cod liver oil, that he was admitted into the hospital. He had slight signs of phthisis at the left apex. After admission he improved a little, gaining 5¼ lbs. in weight by June 14th. His bowels were very obstinately constipated, and towards the end of June he had some gastric trouble for which all his medicines were stopped except an occasional purgative dose of jalap.

On July 4th, he complained of faintness; as we were on the look out for the supervention of coma, his urine was tested with ferric chloride and found to give a marked colour reaction which disappeared on heating.

On July 8th he went out to see his mother who lived in the town; the next day he complained of feeling very tired and did not eat his food. On that day also the ferric chloride reaction was present.

On the evening of July 10th he said he was feeling very tired, and complained of sharp pain in the left side of the chest with difficulty of breathing. This was relieved by hot fomentation. The following day he was still tired and *drowsy;* his hands and feet were cold. Towards evening *his respirations became deep, and sighing,* he was cold and drowsy, but could be roused, and answered questions intelligibly. He died quietly at 7 a.m.

The *post mortem* examination was performed the same day by Dr. Foxwell. The brain weighed fifty-nine ounces; there was a cyst the size of a horse bean in the white matter of each frontal lobe, and the lateral ventricles were dilated and contained clear fluid. At the apex of the left lung were two small cavities, and the lower lobe was in a state of recent pneumonic consolidation. There was no unusual smell on opening the body, but the blood which ran out as the organs were removed was of a milky purple colour. On standing it looked like black currant juice on which cream was floating. Under the microscope the cream-like layer consisted of finely molecular matter, entirely soluble in ether. Some of the blood was distilled by Dr. MacMunn, but no *acetone* could be detected in the distillate. The liver weighed 81 oz., it was soft, friable, and its cut surface was mottled with yellow patches. The spleen weighed 5 oz., and appeared normal. The pancreas weighed 1½ oz., it was only 4 inches long, and very friable. The kidneys weighed together 18 oz., they were coarse, pale, and soft, their capsules stripped off readily. The suprarenal capsules were healthy. The semi-lunar ganglia were much enlarged, and of dense consistence. The large intestine was stuffed full of solid fæces.

The semi-lunar ganglia were hardened in picric acid and examined microscopically. The sections showed great increase of connective tissue which was swollen and hyaline, and crowded with lymphoid cells. The nerve fibres were abundant, and their nuclei well marked. The ganglionic cells were loaded with pigment but otherwise unchanged.

The lungs, liver, and kidneys were examined microscopically for fat embola. The lungs presented no branching embola, but in some cases the capillaries contained droplets of fat large enough to occlude the lumina of the vessels. The liver capillaries contained numerous similar droplets. The connective tissue of the liver around the ducts showed some infiltration with round cells. The kidneys were very slightly fatty, some tubules contained hyaline casts, and there was an increase of connective tissue around the larger veins. The capillaries contained very few fat droplets on the whole; by far the largest amount of fat was seen in the capillaries of the liver, and this to such an extent as to suggest very strongly that it was formed there.

I examined the heart very carefully for glycogen, following Frerichs' directions, but the muscular fibre, though showing a considerable degree of pigmentary or brown atrophy, was otherwise free.

CASE 59.—*Acute Diabetes—coma—death—autopsy.*

F. W. A., seventeen, jeweller, presented himself as an out-patient at the General Hospital, on Thursday, Oct. 19th, 1882, complaining that he was rapidly losing strength and flesh, and passing a very large quantity of urine. He looked very ill, and his urine, on examination, contained a large quantity of sugar, was of sp. gr. 1040, but gave no reaction with ferric chloride. He was recommended for admission, and the following

history was obtained. There was no known instance of diabetes in the family; his mother died of phthisis three months ago, and this circumstance had been a source of great grief to him. His previous health had been good, with the exception of bilious attacks, to which he was subject. Five weeks ago, he began to feel ill and to pass water during the night, and for the last fortnight he had been passing very large quantities both in the day and night, altogether, he estimated, about two bucketsful of what he described as "hay-smelling" urine. For the last two weeks he had suffered from constant frontal headache, and great thirst; his appetite had continued good, but not inordinately so. His bowels during the same period had been open every other day. Five days ago he vomited, and had to give up his work. His penis became a little sore, and he noticed that his urine left a sticky stain on his shirt. He had been taking medicine from a chemist for four days before admission.

Present Condition, October 20th, 11 a.m. (the day after admission):—Patient complained of frontal headache, weakness, constant desire to pass water, and great thirst. He was an emaciated looking lad, with dilated pupils, and dark rings under his eyes; his alæ nasi were working, but his lips were of a good red colour. Expression anxious; skin dry and rough; Temp. 98°; Pulse, 112; Respirations, 24. No œdema of legs. Teeth glazed; gums red and slightly spongy; throat covered with thick mucus; fauces reddened; tongue very dry, and its centre coated with a grey fur; appetite fair, no vomiting. Bowels were opened on the day before admission (October 18th). His breath smelt sweet; there was no cough; breathing deeper than in health. The circulatory organs appeared normal. During the night he passed a large quantity of urine, which was acid, sp. gr. 1040, contained $\frac{1}{6}$ column of albumen, and a large quantity of sugar. The urine passed in the morning was acid, clear, greenish coloured, sp. gr. 1035, contained $\frac{1}{8}$ column of albumen, a large quantity of sugar, and gave an unmistakable deep vinous-coloured reaction with ferric chloride. His eyesight was unaffected. On the day of admission the patient took ordinary diet, but since then diabetic diet.

The detection of the ferric chloride reaction at once suggested the fear that coma might be imminent, and as the bowels had not been moved for forty-eight hours, two scruples of pulv. jalapæ co. were administered at 12.30 p.m., and he was ordered to be carefully watched.

3 p.m.—Patient became very restless, and complained of great pain in his abdomen; his respirations were deeper, and his pulse quick and feeble. The pain in the abdomen was relieved somewhat by hot fomentations. The bowels had not been moved.

5 p.m.—Pulse 156, feeble; Resp. 34. Ordered a teaspoonful of brandy every half-hour.

5.30 p.m.—No cyanosis: respirations deep and sighing; pulse very feeble; complained of no pain. Not restless, seemed rather drowsy. Ordered three teaspoonfuls of brandy at once, and a teaspoonful every ten minutes.

7 p.m.—Patient quite comatose: thirty minims of ether injected subcutaneously did not rouse him, nor did he appear to feel the operation of having a drop of blood taken from his finger. After a little he roused sufficiently to put out his tongue and to say that he felt short of breath, but no pain. There was no cyanosis; breathing was very deep, 41; pulse (before the ether) 174, extremely feeble. Pupils were dilated, but reacted to light. Breathing very harsh: heart sounds scarcely per-

ceptible. The blood on examination did not contain any fat globules, but the leucocytes appeared slightly increased. An enema of one ounce of brandy and a drachm of ether, in two ounces of water, was then administered, and he was enveloped in a hot pack.

9 p.m.—Patient had been very violent, tossing himself about in the bed: radial pulse not to be felt; pupils dilated and insensible to light. Breathing deep; no cyanosis. He was deeply comatose and could not be roused. Later on his father managed to rouse him by repeated shouting, and on his father saying, "Do you hear me?" patient replied, "Yes! I hear you."

11 p.m.—Patient died; eight hours after the onset of the more serious symptoms. The nurse reported that he turned "bluish" and struggled very violently before his death.

No urine was passed after 6 p.m.; but ten ounces were passed during the previous hour; this was examined by Dr. Windle, and he reported it to have been pale yellow, clear, acid, sp. gr. 1030, containing a trace of albumen, 1·6 per cent. of sugar, ·95 per cent. of urea; chlorides diminished; no trace of indoxyl; a deep vinous red reaction with ferric chloride.

The total quantity of urine passed in the twenty-four hours, from 5 p.m., October 19th, to 5 p.m., October 20th, was 160 ounces. The temperature on the evening of the 19th was 100° Fahrenheit, but fell gradually, being 98° on the morning of the 20th, and 97° at 7 p.m., four hours before his death.

AUTOPSY.—The *post mortem* examination was performed by Dr. Windle, on October 21st, fifteen hours after death.

External Appearances.—The body was that of a young male, somewhat emaciated; cadaveric rigidity and hypostatic congestion were well marked.

The *Spinal Cord* presented no abnormal naked eye appearance.

Head.—The cranial bones were very thin; the dura mater was extremely adherent; there was no clot in the superior longitudinal sinus. There was increase of the Pacchionian bodies on the arachnoid along the longitudinal fissure. The brain substance was firm, slightly hyperæmic throughout, with numerous puncta cruenta; a small amount of reddish serum in the lateral ventricles.

Thorax.—The cavities of the heart contained some dark fluid blood, and a very few soft clots; the valves were normal; the heart substance was rather pale. The lungs, when squeezed, emitted a peculiar sour acetone-like odour, which was also observed on section of them. Their substance was slightly hyperæmic, but otherwise normal.

Abdomen.—The stomach and intestines were much distended. There was no unusual smell detected on opening this cavity. The diaphragmatic concavity reached as high as the upper edge of the fifth rib. The liver was slightly enlarged, and on section pale in colour. The gall bladder was almost empty and collapsed. The bile ducts were pervious. The spleen was small and soft. The kidneys were rather large, their capsules stripped readily; substance pale. The supra-renal capsules were normal. The pancreas was small and shrunken in appearance. The stomach was full of pultaceous food; its mucous surface showed patches of hyperæmia. The intestines were loaded with fæces, the sigmoid flexure and rectum being stuffed full of hard grey masses, quite uncoloured by bile. The small intestine was full of pale yellow soft

fæces. There was a large mass of tænia in the colon. The solar plexus and cervical sympathetic ganglia appeared normal. The blood nowhere presented any abnormal appearance.

On microscopical examination the liver, spleen, kidneys, and lungs were quite normal. There were no fat embola or any traces of fat in the vessels of the lungs and kidneys, or in the renal tubules. The medulla was also normal, though the perivascular spaces were slightly enlarged. The cells of the pancreas were badly defined, and their contents cloudy. The sympathetic ganglia were unfortunately lost.

Dr. Norris, who examined the blood, reported that the leucocytes were peculiarly large, and the red corpuscles and granular matter slightly in excess, but there was no excess of fat.

The clinical phenomena presented by this case are of great interest. In the first place, the diabetes was apparently produced by nervous shock, the profound grief induced by the death of a near relative, a fact which is in accordance with many previous observations, and which goes with them to support the view of the purely nervous origin of the disease. Secondly, the course of the disorder was remarkably acute and rapid. Thirdly, we were able to trace the development of the whole of the terminal symptoms.

Among the earliest of the premonitory signs was the alteration of the respiration: in the morning note we find that the breathing was "deeper than in health."

Throughout the report of the clinical symptoms we have repeatedly the note, "no cyanosis," and until just before death, when according to the nurse he turned "bluish," there is not the slightest evidence of any alteration in the function of blood aëration. Undoubtedly cyanosis has been described in other cases, but as it is not constant, when present it is probably due to some complication. Its absence indicates that the dyspnœa is purely nervous in origin, and the result of stimulation of the respiratory centre, rather than of any local change in the lungs, and this affords an additional argument against the theory of Sanders and Hamilton.

The *pulse* at the morning visit was 112, and soon rose to be extremely rapid and feeble; this symptom is of great value as an early indication of the onset.

Abdominal pain was complained of first at 3 p.m., and may have been partly the effect of the purgative; but it is, however, known to be a very constant and early sign in these cases.

Drowsiness was first noticed at 5.30 p.m., and by 7 o'clock he was quite comatose.

Death was preceded by *convulsions*. Senator speaks of twitchings as sometimes supervening, but in another case

under my care as in this, actual convulsions occurred. Convulsions have also been observed by Minot and by Buhl. Cyr considers that the absence of convulsions affords a diagnostic distinction between this form of coma and that from uræmia, but this, it is obvious, cannot be maintained.

Among the premonitory signs presented by this case, were the gradual fall in the sp. gr. and quantity of the urine, and consequent diminution of the amount of sugar excreted, which was far too great to be accounted for by the change of diet. In the last sample of urine examined the quantity of sugar was only about seven grains to the ounce, an amount which must have been greatly surpassed in the previous day, when the sp. gr. was ten degrees higher. A sample of the urine, some days old, was distilled by Prof. Tilden, F.R.S., at Mason College, for acetone, but none was found.

The percentage of urea was low, being under one per cent., but considering the large quantity of urine passed, the total amount excreted during the final twenty-four hours of life must have been quite seven hundred grains. This disposes of the suggestion that the toxic phenomena were due to non-elimination of urea. No urine was passed after 6 p.m., but this coincided with the supervention of the coma.

This case illustrates the prognostic use that may be made of the ferric chloride reaction, for although it is not uncommonly found in diabetes without being followed by coma, and is often present in the urine of other diseases, yet its sudden appearance, especially in young subjects and in acute cases of diabetes, should be regarded as a sign of grave moment, and should direct attention to the state of the bowels, the respiration, the pulse, and the other prodromata which have been described.

The *temperature* as a rule is normal, or subnormal, but it may rise to a considerable height (Case 63).

CASE 60.—*Diabetes Mellitus—intra-venous injection—death from coma with high temperature.*

Sarah L., nineteen, tailoress, was admitted on August 22nd, 1885, complaining of thirst and of passing a great quantity of water.

Condition on Admission.—She was poorly nourished, but the physical signs were normal. The urine was 136 oz., sp. gr. 1039, acid, clear, a cloud of albumen; sugar 7·6 per cent.; urea 0·65 per cent.; acetone and ferric acid chloride reactions both well marked. Temp. 98·8°, Pulse 108, Resp. 24. She was placed on house diet and ordered a simple enema.

Progress of Case.—On the evening of the 23rd she had an enema, and

felt faint after it. She vomited just before midnight, and again at 4 a.m. At 5 o'clock she cried, and complained of great pain in the small of her back. The matter vomited gave a distinct acetone reaction with the nitro-prusside test. Hot fomentations were applied, and at 8 a.m. she had a grain of extract of opium, and a second was given at 10 o'clock. At the visit at 10 a.m. she was still complaining of the pain; her respiration was panting, 32; pulse 132; temp. 98·5°; bowels had been moved freely; tongue red and dry. She had passed no water since 4 a.m., so at 11 a catheter was introduced and 10 oz. of urine drawn off, which was pale, clear, sp. gr. 1040, acid, with a cloud of albumen, sugar 5·9 per cent., urea 0·9 per cent., acetone and ferric chloride reactions well marked. She was becoming unconscious, and by 11.30 was lying on her back comatose, with contracted pupils. At 11.30 thirty-six oz. of sulphate of soda solution were injected into the veins. She improved during the operation, the pulse became stronger, she was less drowsy, and she complained of the tightness of the bandage which had been applied to her arm. At 2 p.m. she could not swallow, so three-quarters of a pint of water were administered by the bowel. At 3.30 the pulse was 165, very feeble, eyes turned up, respiration sighing. At 4 p.m. a second enema of about a pint of acidulated water was given. The pulse improved a little and respiration was quieter. At 5.30 sixteen oz. of urine were drawn off, which did not differ materially, except that it was of sp. gr. 1031, and contained only 4 per cent. of sugar and 0·3 per cent. of urea. An enema of acidulated water was given every hour; but at 7.30 p.m. the noisy deep breathing began again, and the enemata were discontinued as they were not retained. At 7 p.m. the temp. was 130°, and at 9 p.m. it had risen to 103·5°. Resp. 22; Pulse 169. No other change took place. She died quietly, without any convulsion, at 11.10 p.m.

At the autopsy the body was covered with a thick layer of fat. There was no peculiar smell on opening the body. The blood appeared normal. All the internal organs were congested but healthy, though the brain presented some excess of cerebro-spinal fluid.

DIAGNOSIS.—I do not think anyone can find a difficulty in diagnosing diabetic coma, when he has once grasped its salient features. The peculiar dyspnœa, which is so characteristic, at once arrests attention. This is regarded by Senator as a pathognomonic symptom, and our present knowledge justifies his view. But it is not so easy, and, if possible, it is of greater practical importance to recognise those prodromata which foreshadow the approach of these formidable and almost invariably fatal symptoms.

The first warning of their supervention has been, in two cases of my own, the discovery of a very marked ferric chloride reaction in the urine. In Case 58, it was very remarkable that this reaction, which had been repeatedly looked for, was never noted till just before his death. I think, therefore, that restricting this statement to cases of diabetes, the sudden occurrence of this reaction should

always serve as a warning. Stadelmann attaches much prognostic importance to the increase of the ammonia in the urine.

Rapid disappearance of sugar from the urine has preceded the attack, but this is exceptional, as is also any marked alteration in the quantity of urine. Of more certain value than any of the foregoing is *epigastric pain.* This often precedes by some hours any other symptom. Next to this, in chronological order, is *rapidity and feebleness of the pulse.* But most significant of all is the *altered respiration.* Inspiration and expiration become prolonged, and the respiratory rhythm is quickened, but air enters freely into the chest; the lips and cheeks retain their former colour. Sooner or later the patient becomes *drowsy*, but it is easy to awaken him from this somnolent state. Convulsions may appear, usually towards the termination of the case; and before death cyanosis may be present, from failure of the circulation than from any difficulty in the oxygenation of the blood in the lungs.

The peculiar odour of the breath is so far from being a constant phenomenon that Küssmaul did not mention it in his description, and I believe it to be present only in a minority of cases.

PROGNOSIS.—The prognosis of these cases is most grave, but although the serious disorders so generally present almost preclude recovery, it is right to remember that four cases have been recorded in which death did not take place (QUINCKE, GAMGEE, REYNOLDS).

The two following examples show that epigastric pain, drowsiness, and even sighing breathing, are not necessarily followed by fatal coma.

CASE 61.—*Diabetes Mellitus—polyuria—thirst—wasting—temporary attacks of drowsiness—early loss of sexual desire—urethral pain—no benefit from treatment—discharged at own request—death soon after.*

Charles S., thirty-six, chaser, was admitted into the General Hospital on December 12th, 1889, complaining of polyuria, thirst, loss of flesh, and pains in the back and thighs. These symptoms began twenty-five weeks ago with frequency of micturition, followed in a week or two by pains between the shoulders, for which he consulted a doctor, who told him he had diabetes, and put him on a diet under which the quantity of his water became less, the frequency of micturition was diminished, and the pain in the back disappeared. In fact, he was so much better he was allowed to take bread and potatoes; but this was only for one day, as the doctor stopped them again. Latterly he had begun to get very low; his

urine had increased again in quantity. He left off work and seemed to improve, but again became worse. On October 21st, he attended as an out-patient, and for the next month improved, gaining weight and passing less water; but he relapsed, and continued to get worse until admission. In the course of his illness he had several attacks of drowsiness, which passed off in two or three days. Sexual power disappeared very early, but returned for a short time at the end of six weeks.

Previous History.—He attended the Queen's Hospital when eleven years of age with a cough, and at twenty-eight he had a quinsy. He also had small-pox and measles when a child. He could remember no accidents or injuries.

State on Admission.—He was a well-developed but spare man, with some varicose veins in his legs. No jaundice or œdema, or skin eruptions. Complained of lumbar pain on admission, which disappeared after twenty-four hours' rest in bed. Skin dry, weight 8 st. 3 lbs.

Alimentary System.—Lips dry, with teeth decayed, tongue moist and pale. Appetite good but not excessive, thirst great. Mouth dry and sour in the morning. No pain or tenderness in abdomen. Liver dulness in V. M. L. 2½ inches.

Circulatory System.—Heart's area not increased; apex beat in fifth I. S., internal to V. M. L. Heart-sounds weak but clear. Pulse fairly strong and regular.

Respiratory System.—Respiratory muscles wasted, showing fibrillary contraction when tapped. Movements normal. No cough. Physical signs normal.

Genito-urinary System.—Sexual desire absent; no irritation of genitals. Urinated once every hour and a half, with sharp pain in the middle of urethra, which lasted about three minutes. Stream good but twisted. No history of gonorrhœa; no difficulty in passing water. Urine 188 oz., acid, straw colour; urea 1·27 per cent., no albumen; sugar 4·7 per cent.; acetone present.

Nervous System.—Aching pain in thighs, worse in bed. Eyesight and hearing good. Sleep unimpaired.

Treatment.—Diet: meat, fish, fowl, green vegetables, 1½ pints of milk, 1 pint of beef tea. Medicine: *Ext. jambolanæ liq.* (Christy) ℥ij.; *tr. opii* ♏xv.; *aquam* ad. ℥j.; thrice daily, with *ext. cascaræ liq.* ℥ss.; *glycerini* ℥ss.; *aquam* ad. ℥j.; at bedtime as an aperient.

Dec. 16th. Complained of pain in epigastrium and bitter taste in mouth, with drowsiness.

17th. Drowsiness, pain, etc., had gone.

31st. He went home at his own request, and we heard that he died very soon after.

The following table shows the effect of treatment.

DATE.	URINE.	SP. GR.	UREA.	SUGAR.	WT. OF PATIENT.
Dec. 13th....	188 oz.	1032	1·27 p.c.	4·7 p.c.	8 st. 2 lbs.
„ 16th....	136 oz.	1030	1·5 p.c.	4·0 p.c.	
„ 19th....	160 oz.	1028	1·1 p.c.	3·7 p.c.	8 st. 1½ lbs.
„ 25th....	168 oz.	1035	1·1 p.c.	5·5 p.c.	8 st. 2¼ lbs.

CASE 62.—*Diabetes Mellitus—polyuria—thirst—wasting—threatening coma averted by spontaneous diarrhœa.*

William S., aged twenty-one, engine cleaner, was admitted into Hospital on March 27th, 1887, complaining of thirst, loss of flesh and polyuria.

History.—His illness began six weeks before with thirst. He had a "low fever" three years ago, and formerly suffered from some kind of urticaria when working as a brass filer. He had always been temperate, and had a comfortable home. Father and mother and all his brothers and sisters alive and well; no history of diabetes in his family.

Condition on Admission.—He was rather deaf, especially in the left ear. He was wasted, and looked ill. Except some dulness and deficient breathing at the left apex posteriorly, the physical signs were normal. Urine 250 oz., sp. gr. 1037, acid, pale straw colour, no deposit, 0·8 per cent. of urea, 6·2 per cent. of sugar, a faint trace of albumen, a few squamous epithelial cells and crystals of oxalate of lime.

Progress of Case.—On March 31st he was dieted and treated with alkalies. His urine fell to half the quantity.

On April 3rd he complained of pains in head and abdomen, seemed drowsy, and had sighing breathing. His bowels, which had been acting once daily, were moved spontaneously four times, and the condition passed off.

He left at his own request on April 18th, and we heard in July that he had died.

TREATMENT.—Prevention is proverbially better than cure, but I need not repeat what has been already said respecting the predisposing and exciting causes, and will assume that all possible means will be taken to guard against them. In addition, two plans of treatment by drugs suggest themselves as theoretical prophylactic measures. The first is to check the fermentative processes by means of antiseptic or antizymotic drugs. For this purpose Foster recommended thymol, but I am not aware that he has ever given it a trial. Salicylate of soda has been used very extensively in diabetes, but in spite of it these symptoms have supervened. Nevertheless, in selecting new remedies we should bear in mind that this action of the salicylate is one among other reasons for its employment.

The other plan is the use of alkalies. This mode of treatment has received the sanction of the highest authorities, yet it is at present in some danger of falling into disfavour. A high degree of acidity of the urine should be regarded as an indication for its use, Vichy water being as good as any other mode of administration.

Is there any remedy which can arrest the attack, when it has commenced?

Frerichs regards all therapeutic measures hitherto suggested

as useless. Injections of ether, camphor, and similar stimulants have been tried without advantage.

Küssmaul tried transfusion of blood with only temporary results, and inhalation of oxygen was also without effect. Bence Jones employed peroxide of hydrogen and stimulants with no better result. Hilton Fagge and Taylor injected a weak solution of phosphate of soda and sodium chloride into the veins, in one case with benefit for some hours, but after a dose of codeia the coma returned and proved fatal. In another case no result followed. Reynolds recommended, and published two cases of recovery after the administration of a dose of castor oil followed by thirty to sixty grains of citrate of potash every hour in copious draughts of water, the patient being encouraged to drink about a gallon. None of these has proved itself worthy of our confidence.

Rest in bed should always be insisted on when any threatening symptoms appear. In the early stages I recommend energetic evacuation of the bowels, and the administration of stimulants and alkalies by the mouth or rectum.

These three cases further illustrate the results of various remedies.

CASE 63.—*Diabetes Mellitus—polyuria—thirst—emaciation—coma—use of strychnine—high temperature—death—autopsy.*

Arthur P., forty-three, nailer, was admitted into the General Hospital on October 20th, 1886, complaining of thirst, weakness, and of passing a large quantity of water—he thought as much as six or seven quarts a day.

History.—His illness began six months ago with pains in his legs, which his doctor called rheumatism. A month later it was discovered that he had diabetes, but no change was made in his diet. He continued to get worse, and having been to Rhyl without benefit he came to the hospital. His previous health had been good, except for rheumatic pains in his hands. His father and mother were alive, as well as all his brothers and sisters, and, except that his mother suffered from rheumatism, no pathological incident could be discovered.

Condition on Admission.—He was a small, emaciated man; height 5 ft. 3 in.; weight 8 st. ½ lb. He used to weigh 10 st. Temp. 98°; Pulse 72; Resp. 14. Teeth irregular and decayed, tongue red and beefy, flatulent eructations after food, bowels regular, liver and spleen normal. Complains of giddiness, and is short of breath on exertion. Heart's sounds normal: no cough; some impaired resonance, harsh breathing, prolonged expiration, and slight crepitation at the right apex. Urine 264 oz., sp. gr. 1035, acid, clear, urea 0·7 per cent., very faint cloud of albumen, sugar 6·9 per cent.

Progress of Case.—On Oct. 22nd he was put on six pints of skim milk daily.

Oct. 23rd. He grumbled about his diet.

Oct. 24th. Complained of feeling low; bowels open; tongue still raw and beefy. Urine 216 oz., sp. gr. 1033, acid, pale, straw colour, white flocculent deposit, urea 0·9 per cent., a cloud of albumen, sugar 6·25 per cent., a trace of blood, and a few red and white blood corpuscles seen with the microscope. At 7.30 p.m. he complained again of feeling low, and of a pain in his bowels which he attributed to the milk.

Oct. 25th. In the morning he made the same complaint, and said he was cold. His pulse was feeble, and his tongue dry, brown, and cracked. At 10 a.m. he was drowsy, and his respiration was rather deep. At 11.30 a.m. Pulse 160; Resp. 20; there was pain in the stomach and bowels; no urine passed since 8 a.m. He was ordered an enema to empty the bowels, a bottle of Vichy water to be taken with lemon juice in the course of the day, an alkaline injection (*Sodii bicarb.* ℥i., ad. *aq.* ℥ss.) to be given by the bowel as soon as the rectum had been cleared out, and the following mixture every hour: ℞. *Etheris sulphuris* ♏xx; *Potassii bicarbonatis* gr. x; *Aquam ad.* ℥i., M. In the course of the day the rectum was well cleared out and scybalæ removed, but he got worse, and at 8.45 p.m. I saw him again. Temp. 99°; Resp. 24. He lay apparently asleep, but could not be roused. His breathing was very deep, but there was no special odour about him. His urine gave a well-marked acetone reaction. He was ordered liq. strychninæ ♏ v. *sub cute* every fifteen minutes until muscular twitchings were produced. After three injections he spoke, and drank some Vichy water. At 9.25 he had another alkaline enema, containing one ounce of bicarbonate of soda. After this the strychnine injections were given irregularly at 10.10, 10.40, 11.10, 11.55, 1.50 a.m., and then not till 9 a.m.

26th. At 9.30 a.m. I saw him again. No physiological symptoms had been produced by the strychnine, so ten minims were ordered to be injected every half-hour. Pulse 128; Resp. 26; Temp. 99°. He was decidedly better, answered when spoken to, took beef tea very well. The knee jerks were absent. The strychnine was again neglected; after I left it was given only every hour. His temperature had begun to rise. At 11.30 it was 102°; at 12.30, 103°; by 2 p.m. he was comatose again. Three ounces of urine were drawn off from his bladder; it was acid, sp. gr. 1023, and free from albumen and sugar. At 5 p.m. his temperature was 105°, and at 6 p.m. reached 106°. At 6.30 he was plainly dying; the face was a little drawn to the left, and the right pupil was larger than the left. He died at 6.40 p.m. without any other change taking place.

AUTOPSY.—A spare subject, somewhat emaciated, faint sweetish ethereal odour emanating from cadaver, p.m. rigidity slight, hypostasis chiefly posterior.

Brain Membranes.—Excess of serous fluid in subarachnoid space and in ventricles; arachnoid very œdematous, cerebral convolutions well defined, no change to naked eye.

The corpora striata and optic thalami showed no change on section except the "pin holes" described by Dickinson; these were certainly evident and scattered chiefly in the white substance of the internal and external capsule. Medulla: no change recognisable by naked eye; it was kept for microscopic investigation. Pons normal.

Heart—8 oz., normal.

Lungs.—*Left* upper lobe solid with caseous pneumonia; the interlobular peribronchial fibrous connective tissue was likewise thickened. Pleura over upper lobe thickened and adherent; lower lobe congested

and œdematous. *Right Lung:* one or two small foci of caseous pneumonia at apex.

Liver.—59 oz., surface of a dark reddish brown colour. Section: the organ was generally hyperæmic, of a dark red colour, but scattered here and there in an irregular fashion were small yellowish patches corresponding to two or more lobules, where the liver cells microscopically were very fatty.

Kidneys.—10 oz., capsules stripped easily, both very dark from hyperæmia, the streaky and punctiform distribution of which was very obvious; the glomeruli appeared as minute red points, slightly elevated above the surface; the medullary cones were of deeper hue.

There was a faint sweetish ethereal odour emanating from the viscera.

No mention of the condition of the pancreas or semi-lunar ganglia.

CASE 64.—*Diabetes Mellitus—family history of phthisis—acetonuria—coma—strychnine injections—oxygen inhalations—and intra-peritoneal alkaline injections—death—autopsy.*

Mary Ann M., aged thirty, screw-maker, was admitted into the General Hospital on September 10th, 1889, complaining of great and increasing weakness, excessive thirst, and increased secretion of urine. These symptoms came on gradually four years ago, accompanied by low feelings, fainting fits, sickness, and shortness of breath. Her hunger was at that time so great that she could not get enough to satisfy herself, and she began to lose flesh, to sweat a great deal at night, and to suffer from a troublesome itching of the skin, which was worse at night. During the whole time her bowels had been very constipated, having been open only once or twice a week. Micturition had been very frequent and attended by smarting. For the last month there had been some pain and discomfort after food; and her ankles had got swollen after she had been standing. Three days before admission she had felt so low that she had gone to bed, and had remained there ever since.

Family History.—Father alive, but suffering from phthisis. Mother and seven brothers alive and well. Seven other children died young. Patient had been married ten years, but had had no children.

Previous History.—Could remember no other illness.

State on Admission.—Patient was rather a spare woman with a flushed face. Temp. 99·5°; Pulse 88. Weighed 7 st. 5 lbs.; former weight 11 st. 4 lbs. There was a peculiar sweet smell emanating from her.

Alimentary System.—Teeth decayed posteriorly; gums bled readily; subject to toothache; teeth were loose, but had got firmer; a nasty taste in the mouth, worse in the morning; mouth dry; great thirst; appetite voracious. Tongue large, dry, cracked transversely, and covered with thin dirty fur on dorsum. Some pain and discomfort after food. Stomach dilated, reaching nearly to umbilicus, with splashing sound on palpation. Liver dulness 4 inches in V. M. L. Splenic dulness not increased.

Circulatory System.—No pain or palpitation; some dyspnœa. Area of cardiac dulness not increased; apex beat in fourth l. S., inside the V. M. L. Sounds clear; pulmonary second accentuated. Pulse 96, not easily compressible.

Respiratory System.—No cough, pain, or dyspnœa; percussion note deficient in resonance at right base.

Urinary System.—Urine 90 oz., sp. gr. 1034, acid, pale amber; urea 1·1 per cent., a very faint haze of albumen; sugar 5·4 per cent.

TREATMENT.—Diet: Mutton, meat jelly, milk two pints, cold meat two portions, Vichy water with lemon juice. Medicine: *Extracti belladonnæ* gr. ¼; *extracti aloes* gr. iij.; *euonymini* gr. j.; in pill at bedtime.

July 15th. Complained of feeling very sick; ordered an enema, which brought away a motion containing a lot of hard lumps. Urine 1025, highly acid; contained a haze of albumen, gave a deep Burgundy red coloration with ferric chloride, and a moderate rose-violet coloration with nitro-prusside of sodium and ammonia. At *noon*, face flushed, epigastric pain, pulse 132, tongue dry, respiration 24, sighing. Ordered, *liquoris strychninæ* ♏v., *sub cute quartis horis;* and to continue the Vichy water without the lemon juice. Later in the day her extremities got very cold.

July 16th. 4 a.m., was conscious; 8.30 a.m., pulse scarcely perceptible; hands not cold; unconscious; passed water in bed. Respirations irregular, but not Cheyne-Stokes' type. Pulse 128; Resp. 32. 10 a.m., extremities cold. 10.30, passing plenty of water in bed; swallowing difficult. Strychnine to be injected every half-hour. This was done regularly until 4.35 p.m. inclusive, except at 3.30. 11.30. Oxygen was administered by means of a nitrous oxide gas apparatus. During the inhalation the pulse became *weaker*. The whole of the oxygen contained in a cylinder was given, but without the slightest benefit. 3.30 p.m. A solution of bicarbonate of soda (two oz. of the salt dissolved in two pints of water at 100° F.) was slowly introduced into the peritoneal cavity. 4.15 p.m. No result having followed the first injection, two pints more were introduced. The patient seemed better. She took some milk and beef tea; and just as there seemed a ray of hope that at least temporary improvement had been secured, she quite suddenly looked worse, there was a slight spasm of the muscles of face and left arm, and she died in spite of the prompt injection of a syringeful of ether.

AUTOPSY.—A spare but fairly nourished woman. Abdomen distended, and on opening it a large quantity of yellowish tinged fluid escaped. The retro-peritoneal cellular tissue was much infiltrated with fluid, also the deep fascia and inter-muscular connective tissue of the lower part of right side of thorax.

Brain.—46 oz., anæmic, nothing abnormal recognised with naked eye. Pons and medulla preserved.

Heart.—8⅓ oz., L. V. was firmly contracted and appeared thicker than normally, measuring nearly $\frac{7}{10}$ inch. No valve lesions, heart otherwise quite healthy.

Lungs.—2 lbs., both congested; hypostasis of the bases.

Liver.—65 oz., much engorged with blood. Veins dilated. Colour of parenchyma a dark reddish brown, but mottled here and there with yellowish patches.

Kidneys.—15 oz., large, capsules tense, slightly sticky. On section both looked fatty. Cortex increased and variegated by deep red striæ alternating with an opaque yellowish grey labyrinth, both considerably congested.

Pancreas.—2¾ oz., small, gland substance looks shrunken, consistence generally tough and fibroid, cuts with perceptible resistance to knife's edge.

Semilunar ganglia.—Looked small, weighed together 57 grains.

Stomach.—Much distended, partly with a dark brown grumous fluid; mucous membrane pale but remarkably mammillated.

CASE 65.—*Diabetes Mellitus—heredity—vertigo—diarrhœa—acetonuria—sickness—coma—no ferric chloride reaction—intra-peritoneal injections—death—autopsy.*

Amelia P., aged thirty-seven, domestic servant, was admitted into the General Hospital October 23rd, 1889, complaining of hunger, thirst, wasting, and polyuria. These symptoms had existed for ten months.

Previous History.—She could remember no previous illness or injury; her health had been good, but she was subject to frontal headaches. Six years ago she had an "abscess" over the left eye, and the pain had been worse in that spot ever since. She had worn spectacles since she was twelve years of age, and had supported herself since she was thirteen. The work had been hard, and she had had a good deal of worry, but had always plenty to eat. She had been accustomed to take very little beer, about one glass for supper.

Family History.—Father died of bronchitis, aged fifty-three. Mother died of diabetes, aged thirty-seven; in the latter part of her illness she had many "fits." One brother died in the General Hospital after an accident; two others were living in good health. She did not know of any insanity or phthisis or any other case of diabetes in the family.

State on Admission.—A small, slightly developed woman. Weighed 6 st. 10 lbs., but used to weigh 8 stone or more. She looked wasted. Her face was a peculiar brownish yellow colour, which she said was a recent change; her cheeks were flushed and her lips red. Eleven days before admission she had a fit of giddiness in which she fell down and abraded the skin on the bridge of her nose. She believed that she lost consciousness completely. Temp. 97°, Pulse 84, Resp. 18.

Alimentary System.—She was very hungry, craving food every two hours, and her thirst was also great. Bowels regular. Tongue pretty clean, furrowed, dry. Teeth defective, decaying. Flatulence after eating, but no pain or tenderness. She had had one or two severe attacks of diarrhœa. Abdomen not distended. Liver dulness in V. M. L. 3¼ inches. Splenic dulness in M. A. L. 1¼ inches.

Circulatory System.—Heart's area not increased. Apex in fourth I. S. in V. M. L. Sounds normal. Pulse 84, regular, small and soft.

Respiratory System.—Chest movements normal, no cough. Percussion and breath sounds normal.

Genito-urinary System.—She had not menstruated since November (12 months); no vaginal discharge. Frequent micturition. Urine 244 oz., sp. gr. 1035, acid, pale yellow; urea 0·8 per cent., no albumen; sugar 5·7 per cent., acetone present, no deposit.

TREATMENT.—Diet: Meat, beef jelly, fish, chicken, two eggs, no bread or vegetables, toast-water, Vichy water and lemon juice. Medicine: *Ext. opii* gr. j.; twice daily.

Progress of Case.—Oct. 26th. Between 3 and 4 a.m. she had a severe attack of diarrhœa, followed by a feeling of sickness, and was drowsy and heavy all day. Complained of being hot and feverish, but temperature was 98·5°.

Oct. 27th. Complained of sickness and a sinking feeling; ordered half a pint of milk, an effervescing mixture, and some gluten bread.

Oct. 28th. She would not eat the meat alone, so was allowed green vegetables, and as no gluten bread had arrived, two small slices of toast were allowed.

Oct. 29th. Sick again in the morning. Respiration sighing at times towards evening.

Oct. 30th. Was restless and moaning all night. Between twelve and one she was delirious, screaming and trying to get out of bed. Respiration was sighing, 20. Pulse 96. Hands and feet cold; not conscious. No water had been passed since 9 p.m. 11 a.m. she was lying quietly, respiration sighing, face pale, extremities cold; no peculiar odour of breath. Urine, drawn off by catheter, 7 oz., pale, greenish, clear, acid, sp. gr. 1017, a cloud of albumen, loaded with sugar, faint acetone reaction with nitro-prusside of sodium, *no reaction with ferric chloride.* 11.45, almost pulseless; a syringeful of ether was injected subcutaneously. 12.15, two pints of the following solution, at the temperature of the body, were injected into the peritoneal cavity:—*Sodii sulphatis; sodii bicarbonatis* āā ℥j.; *aquæ bullientis* ℥viij.; *solve;* adde aquæ distillatæ, Oj.

This was followed by no improvement, and she died at 2.15 p.m. the same day.

AUTOPSY.—Height, 60 inches; circumference of chest, 27 inches; rigidity well marked; puncture seen in linea alba midway between umbilicus and pubes.

Thorax.—Heart 7 oz.; large milk spot over right ventricle; much fat over right ventricle externally. Left ventricle, heart substance slightly fatty; mitral valve normal; aortic valve normal and competent, commencing atheroma at the beginning of the aortic arch. Right ventricle contained very dark p. m. clot; tricuspid and pulmonary valves competent and normal; auricles normal. Left lung: 8 oz.; substance healthy; no bronchitis; was bound down to chest wall by few adhesions. Right lung: 10 oz.; normal.

Abdomen.—Liver: anterior surface adherent to the diaphragm. On section, consistence rather tough. Groups of lobules appeared translucent surrounded by yellow streaks. Gall-bladder collapsed; on squeezing it yellowish-green bile exuded. Right kidney: 6 oz.; capsule slightly adherent, taking away a little kidney substance; cortex pale yellow; interpyramidal cortex the same, streaked with translucent yellow lines; malpighian bodies very prominent through the whole cortex, arranged in rows; pyramids lightish red, streaked with yellow. Left kidney: 6½ oz.; same condition as right.

Brain.—3 lbs.; subarachnoid fluid over both hemispheres. Section showed brain substance slightly congested. Right semilunar ganglion somewhat larger than left.

CONCLUSIONS.—The following conclusions summarise briefly the most important facts contained in this long chapter:—

1. Diabetic coma is specially apt to supervene in acute cases in young persons.

2. Diabetic patients and their friends should be warned of the danger of constipation, muscular fatigue, nervous exhaustion, and cold, as probably predisposing causes of death by coma.

3. The discovery of the ferric chloride reaction in the urine should be taken as a warning against the premonitory symptoms of coma.

4. Deep respiration, rapid pulse, and abdominal pain are the earliest premonitory signs of this condition.

5. Cyanosis is absent in spite of the dyspnœa, but may appear just before death.

6. Convulsive seizures are not an uncommon occurrence just before death.

7. The temperature is usually normal or sub-normal, but may be considerably raised.

8. Diabetic coma, with all its classical symptoms, occurs independently of any excess of fat in the blood, and the pathological value of lipæmia, when present, is yet undetermined.

9. The toxæmic theory, *e.g.*, poisoning by acetone, or β-oxybutyric acid, or some nearly allied substance or substances, affords the best explanation of this remarkable group of symptoms.

10. Recovery is possible from the prodromal symptoms, and even from some degree of drowsiness, but from actual coma it is at least very rare.

11. Great benefit may ensue in the early stages from speedy evacuation of the bowels by a brisk purgative. Treatment in the later stages seems always unavailing.

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CHAPTER XXI.

TREATMENT OF DIABETES.

THE treatment of diabetes has fortunately been evolved independently of those physiological controversies respecting the pathogenesis of the disease which seem to be as far as ever from an end. The meat diet of Rollo and the gluten bread of Bouchardat were introduced years before Cl. Bernard made his discoveries, and owe nothing to him or his successors, and we ought to be very unwilling to admit the right of either side in this dispute to dictate to clinicians in this department at least. Our modern treatment is based upon two sound clinical observations, viz., the value of nitrogenous diet and of opium or its alkaloids in controlling the symptoms of the disease. But experience has modified the conclusions to be drawn from these observations, and although they constitute the ground-work of every modern system for the treatment of diabetes, we follow neither in its original simplicity.

DIET.—We have learnt that while strictly nitrogenous diet is by no means always able to remove all the sugar from the urine, every diabetic retains the capacity to assimilate a certain amount of carbo-hydrates; moreover while a strictly nitrogenous diet is badly borne by most patients and can rarely be enforced for more than a short time, a suitable addition of carbo-hydrates improves the general health, makes it possible to secure conformity to dietetic rules for any desired time and does not aggravate any of the symptoms of the disease. There has been during the present century a gradual tendency in this direction, and at the present time our differences in practice are not nearly so great as our differences in theory. The orthodox diabetic dietary, as set forth in most text-books, is very varied and liberal when compared with Rollo's exclusive meat diet, and if we venture to-day to go a step further and claim for each diabetic as much liberty as experience shows he may be safely allowed, it is only in harmony with those general principles which we admit when we declare that we try to treat, not the disease, but the patient, and to adjust our remedies and our doses to his individual wants.

When a case comes first under observation and the diagnosis has been made, it is very desirable to find out the effect of diet; for this purpose the strict anti-diabetic diet should be ordered (*see page* 359). Of course there may be occasions, as in acute disease, extreme weakness or impending coma, where such an investigation would be out of place. But in most cases this should be done, and the patient be requested to adhere closely to the diet for seven days; he may be encouraged to do this by the promise that these rules will be gradually relaxed as his condition permits it. At the end of a week the urine must be collected for twenty-four hours and the total daily amount of sugar calculated in grains. We may then make an addition of some carbo-hydrate, and I know nothing safer or more agreeable to the patient than a large baked potato to be eaten at dinner. Lævulose, in quantities up to 1½ oz. daily, is much appreciated, especially by children. When these have been shown to be tolerated, we may in all but the most severe cases try the effect of permitting bread in the form of thin, very dry toast, of which 1½ oz. may be allowed three times a day.

The effects of each of these additions must be ascertained by careful estimation of the total daily quantity of sugar eliminated at least once a week.

The following examples illustrate this method of proceeding and show that patients who pass a large quantity of sugar on an ordinary diet may pass very little when taking a properly limited amount of bread and potatoes.

CASE 66.—Mr. T. S. W., aged 55, is engaged in large commercial transactions; a moderate case of diabetes in an elderly man. On ordinary diet, urine 84 oz., sp. gr. 1025, contains 2016 grs. of sugar; on strict diet, urine 78 oz., sp. gr. 1018, contains a mere trace of sugar. On adding to this diet one large baked potato and 4½ oz. of toast, estimated to contain about 1500 grains of starch, the urine contained only 2½ grains of sugar per ounce, or not more than 250 grs. of sugar at the outside.

CASE 67.—Mr. D., ætat 50, a slightly more severe case of the same type; on ordinary diet passed 3360 grs. of sugar; on strict diet 576 grs., and on the same with the addition of toast and potato, as described, 672 grs., that is the addition of 1500 grs. of carbo-hydrates caused an increase of less than 100 grs. of sugar!

CASE 68.—Mrs. B., ætat 49 :—

	Urine.	Sugar.
On ordinary diet - - -	70 oz.	3360 grs.
On strict diet - - - -	50 oz.	a trace
„ „ with one potato -	50 oz.	28 grs.
4½ oz. of toast added - - -	50 oz.	360 grs.
4½ „ „ „ - - -	55 oz.	242 grs.

Such cases are of course readily amenable to treatment, but the following are more serious examples:—

CASE 69.—E. C., aged 33, ill ten months, has lost two stone in weight, under strict treatment. Urine, 130 oz., sp. gr., 1028, contains 1872 grs. of sugar. On adding first one then two baked potatoes to his daily diet he improved in health and the sugar fell to 1056 grs. daily.

CASE 70.—K. M. C., aged 8, a tolerably acute case of diabetes with considerable loss of strength, irregularly dieted. On strict diet, kept up with difficulty, daily sugar excretion 1872 grs.; with two baked potatoes daily she gained 7 lbs. in weight, and passed only a trace of sugar.

Several of these cases show that the addition of carbo-hydrates caused some increase of glycosuria, when compared with strict diet, but in every instance it is obvious that the increase only represents a small part of the carbo-hydrate ingested, the balance having been used up in the body.

The effect of strict diet in controlling glycosuria is a very valuable measure of the severity of the case and an indication how far we may safely go in adding carbo-hydrates. That is to say, the less the effect, the smaller room is there for any such addition and the greater the need for caution in proceeding.

Strict Diet.—By this I mean a dietary which is by no means free from sugar-forming substances, but one as free as it is desirable to insist upon. I give my patients a printed slip of paper upon which the following list is printed: Meat soup, beef tea, fish of all kinds, butcher's meat, poultry, game, eggs, green vegetables, seakale, celery, salad, milk (1 pint), cream, custard, butter, cheese, cream cheese, jelly, isinglass blanc mange, Irish or Iceland moss, Callard's brown loaf or almond biscuits, tea, coffee, claret, still moselle, hock, brandy, whiskey, mineral waters; and a footnote points out that no sugar must be employed in the preparation of any of these articles, but saccharin may be used if desired. Fat of any kind, fat bacon, butter, cream, or even cod-liver oil may be allowed with advantage on the strictest diet, although unhappily in severe cases the power of assimilating fat is often greatly diminished.

It is a most important and difficult question how to supply diabetics with a suitable bread substitute when they are unable to assimilate a minimum quantity of ordinary wheaten bread. There is no lack of articles purporting to supply this want, but they vary as the following analyses show, and some, as the *Lancet* has pointed out and I have unhappily too often observed, are neither more nor less than frauds, while the best

are very expensive, so as to be quite beyond the reach of the poorer classes.

ANALYSIS OF GLUTEN BREAD.

	French.	English.
Moisture	9·30	9·0
Sugar	2·50	1·0
Fat	2·50	14·3
Insoluble carbo-hydrates..	33·28	27·4
Gluten	49·62	55·5
Ash	2·80	1·8
Samples dried at 212°:—		
Gluten	54·71	55·5
Insoluble carbo-hydrates...	36·60	27·4

I have quite given up the use of gluten bread as the best contains nearly 30 per cent. of starch; it is always unpalatable and relatively to its dietetic value absurdly dear. In those cases where I wish to try the effect of strict diet I recommend Callard's starchless brown loaf and biscuit food, or biscuits made with almond flour or cocoa-nut flour, to which a little gluten flour or aleuronat flour * may be added.

ANALYSES OF CALLARD'S BROWN LOAF AND BISCUIT FOOD.

	Brown Loaf.	Biscuit Food.
Moisture (212° F.)...	39·50%	8·4%
Mineral matter	3·30	2.5
Fat	34·00	12·5
Starch	6·75	6·6
Nitrogenous matter	16·45	66·6
Cellulose		3·4

The following directions may prove useful to patients who wish to make such biscuits or cakes at home :—

(1,) *Almond Cakes.* One pound of ground almonds, four eggs, two tablespoonsful of milk and a pinch of salt are required. Beat up the eggs and stir in the almond flour, divide into cakes and bake in a moderate oven for forty-five minutes.

* Aleuronat is the patent name of a gluten flour obtained as a by-product in a starch factory. It is strongly recommended by Prof. Ebstein and can be obtained from the diabetic food shops.

(2,) *Cocoa-nut Cakes.* Three-quarters of a pound of dried cocoa-nut, one quarter of a pound of ground almonds, six eggs, and half a teacupful of milk. Mix as before and bake for twenty-five minutes.

(3,) The same. Half-a-pound of dried cocoa-nut, half-a-pound of aleuronat, four eggs, and a little water sweetened with saccharin. Mix, divide into cakes and bake (WILLIAMSON).

Any of these cakes can be sweetened with saccharine or glycerine. It is of importance that the cocoa-nut and almond flour should be tested by the addition of iodine for starch and by boiling with Fehling for sugar before it is used, as adulterations are common.

Certain writers have ventured to recommend Semolina and "Florador" as suitable for diabetes, but the untrustworthiness of the advice is shown by the following analysis:—

	Semolina.	Florador.
Moisture	12·2%	11·00%
Mineral matter	1·1	0·8
Fat	0·7	0·25
Carbo-hydrates	74·5	75·55
Nitrogenous matter	11·5	12·40

The use of "Soy" beans was advocated some few years ago by Dujardin-Beaumetz. These resemble the haricot bean, and are obtained from Soya Hispida, a plant originally brought from China and Japan, but now cultivated in Austria. When originally introduced it was recommended on the ground that it contains only 2 per cent. of starch, but this statement is very misleading, as is shown from the following analysis by Professor Kinch, given in Professor Frankland's "Agricultural Chemistry," which I have had verified:—

Analysis of Soy Beans:—

Water - - - - -	11·3
Nitrogenous matter - - -	37·8
Fat - - - - - -	20·9
Carbo-hydrates - -	**24·0**
Fibre - - - - -	2·2
Ash - - - - -	3·8

This great discrepancy is accounted for by the presence of a mucilaginous substance, convertible into sugar, and therefore equally obnoxious to a diabetic.

Articles made from this bean should not therefore be allowed to patients on strict diet; but those on a modified diet may take them if they like. Some of my patients have disliked the flavour and in others their use has been followed by relaxation of the bowels.

Modified Diet.—In severe cases it is necessary to be exceedingly cautious in the addition of starchy food. Lævulose, which was recommended by Külz in 1874, has only recently become available as an article of food. It is now sold in two forms: (1,) as a white, coarse, granular powder, slightly sweet, and perfectly agreeable, the lævulose of Schering and Glatz; (2,) Haycraft's lævulose, a treacle-like substance prepared by Allen and Hanbury. They are equally good and supply carbo-hydrate in a form which diabetics appear able to assimilate in limited quantities (1½ oz.). Testimony to its utility and harmlessness has been borne by several writers as well as by myself, and I think it decidedly preferable to saccharin.

The following table from de Nédats, quoted by Dujardin-Beaumetz, shows the amount of starch in various vegetable substances:—

Rice	74·10 per cent.
Maize	65·90 ,,
Wheat flour	63·00 ,,
Wheat meal	59·60 ,,
Rye flour	59·84 ,,
Millet	57·90 ,,
Buckwheat	50·00 ,,
Wheat bread	42·70 ,,
Oatmeal	39·10 ,,
Peas	37·00 ,,
Rye bread	36·25 ,,
Haricots	36·00 ,,
Jerusalem artichokes	16·60 ,,
Potatoes	15·50 ,,

Potatoes therefore occupy the first place from this point of view, and I have already quoted several cases which show their effects. The three following cases were all severe, two proved subsequently fatal, and the other was quite unable to eat toast, yet they all bore the addition of potatoes well.

CASE 71.—H. G., ætat 36.

DIET.	DURATION.	AVERAGE URINE.	AVERAGE SUGAR.	WEIGHT.
Strict	4 days	135 oz.	5872 grs.	6 st. 13 lbs.
With potatoes	15 ,,	132 oz.	3455 grs.	7 st. 4 lbs.
Strict	13 ,,	136 oz.	4283 grs.	7 st. 4 lbs.
With potatoes	9 ,,	127 oz.	4141 grs.	7 st. 2 lbs.

CASE 72.—A. J.

With potatoes	11 ,,	87 oz.	2376 grs.	5 st. 1 lb.
Strict	57 ,,	84 oz.	2498 grs.	5 st. 5 lbs.
With potatoes	15 ,,	77 oz.	1625 grs.	6 st. 1 lb.

CASE 73.—A. M., ætat 21.

Diet.	Duration.	Avge. Urine.	Avge. Sugar.	Weight.
Strict -	12 days	91 oz.	2053 grs.	9 st. 2 lbs.
With 1 potato	6 „	63 oz.	1989 grs.	9 st. 5 lbs.
„ 2 potatoes	26 „	77 oz.	1798 grs.	9 st. 10 lbs.

Dahlia tubers have been suggested as vegetables, and have been shown to be of service (HALE WHITE), but are not ordinarily available. This difficulty does not apply to Jerusalem artichokes, which may be tried in definite quantities.

Milk may always be allowed, but 1½ pints daily should not be exceeded. The *skim milk* treatment which was at one time in vogue cannot be recommended. But milk is well known to be a valuable article of diet; it contains a certain amount of fat, milk sugar, and lime salts. Toralbo has drawn attention to the great loss of lime salts in diabetes, and Grube has suggested that milk may be useful to compensate for this waste.

Some authors insist on the use of *alcohol* as a substitute for carbo-hydrate, but I have little experience of its actual utility. Most patients wish to take some, and when no contra-indication exists, such as gastritis or albuminuria, I am in the habit of allowing whiskey, unsweetened gin, brandy, Rhine and Moselle wines, Bordeaux claret, and "sans sucre" champagne; of course in limited quantities, such as half a bottle of wine, or from two to four ounces of spirits daily. In very mild cases Bass's beer which contains only a very little sugar, may be permitted, but it must be given with caution, not more than a pint daily, and its effect on the urine determined. Purdy recommends Budai, a Hungarian wine, and the Diätetischer Rothwein as being quite free from sugar. But no restriction should be placed on non-alcoholic beverages which do not contain sugar. It is cruel to interfere with the craving to satisfy thirst, which is the result of the withdrawal from the body of large quantities of water. All mineral table waters are permissible, and those which contain alkaline carbonates do good by helping to keep up the alkalinity of the blood. They may be suitably taken with wine or spirits at meals, or where no alcohol is taken, with lemon juice or a slice of lemon. Hot water poured on a slice of lemon makes a drink which many persons like.

CLIMATE AND MINERAL WATERS.—No one would be so bold as to contend that the climate of every part of these islands is at all times of the year the best that can be obtained by those who have the means to live where they

please, so that although diabetes is not a disease which is influenced specially by soil, altitude or temperature, some patients may enjoy much better general health and derive real benefit in other places than their own homes. I am strongly of opinion that life in the open-air is of the utmost importance; diabetics should therefore, if possible, live where they can be a great deal out-of-doors. But severe cases stand the fatigue of travelling very badly, and there are many others who would be imprudent to leave the comforts of their own homes, the affectionate care of their relatives, and the wise ministrations of a well-tried medical friend, to exchange these for life in hotels or lodgings, and the attendance of strangers. No diabetic should leave home who is not in fair health, and in possession of sufficient means to procure all necessary comforts. In winter such a patient may find a more genial climate than that in which his home is situated at one of our own south coast watering-places, or in Madeira, the Canaries, the Riviera, Algeria or Egypt. He must travel by easy stages and take with him proper food supplies to maintain his dietary while on the journey. If he is a good sailor he will find it better to go all the way by sea, than to travel overland.

In the summer he may go to one of the spas where diabetes is made a special subject of treatment. The nearest of these is Neuenahr, close to the Rhine and only a short distance from Cologne. In this pretty little town he will find himself amongst pleasant health-giving surroundings, in a district which affords innumerable charming walks and excursions, and at the same time he will be able to obtain excellent treatment for his malady. The waters, whose chief constituents are chloride of sodium and the carbonates of iron and sodium, are highly charged with carbonic acid gas, and are not unpleasant to drink. The hotels and gardens are good. The season is from May to October, but July should be avoided on account of the great heat. The district abounds in mineral springs, the celebrated Apollinaris well being only a few miles away, and this as well as many others afford a great variety of good table waters.

But diabetics may and do go to many of the other Rhenish watering-places, and I see no reason why diabetes should not be treated as well, for example, at Homburg as at Neuenahr. Almost identical waters are found at both, the climatic conditions are much about the same, and English

people may prefer a place where they may meet plenty of their acquaintances, and where the hotels conform to English ideas; but after all it is mainly a preference for the local doctor that determines our selection.

Carlsbad, in Bohemia, has a great reputation for the treatment of diabetes, which seems to me to be due in a great measure to the very able physicians who come there during the season to attend the crowds of patients who flock to this favourite Austrian spa. The chief constituent of the waters is sulphate of sodium, and the different springs vary only in the quantity they contain. The place is well situated, the season is the same as at Neuenahr, and a visit there may be made very enjoyable, but the journey is a long one, the regimen is strict, the mode of living German, and prices are very high. Marienbad, its neighbour, is a little Carlsbad, with the same waters, but over-shadowed by its fashionable rival. Carlsbad is eminently the place for diabetes associated with obesity, gastritis or liver disease.

Vichy (Département Allier), the most famous of all French watering places for the treatment of diabetes, is not so popular as it was formerly with English doctors and patients. This is possibly due to the great advances which German medicine has made during the last fifty years, which have deprived France of her former place of proud pre-eminence on the Continent, or it may be that fashion has changed. Vichy is still as charming as ever, its *établissement* as well managed, its waters as suitable, and it is certainly more accessible. The Vichy waters have for their principal constituent bicarbonate of soda, and are highly charged with carbonic acid gas. The season is from April 15th to October 15th, but the great heat in July and August renders these two months unsuitable.

La Bourboule and Châtel-Guyon, both in the department of Puy de Dôme, are not very far from Vichy, and have comparatively modern reputations for the treatment of diabetes. The former is a small village 2790 feet above the sea level. Its waters contain chiefly chloride and bicarbonate of sodium with traces of arsenic, to which last ingredient great importance is attached in the treatment of diabetes. Châtel-Guyon is a small town, 1300 feet above the sea. Its waters resemble those of Carlsbad, but are weaker and highly charged with carbonic acid gas; they vary in temperature from 82° to 95° F.

Contrexéville in the Vosges is a somewhat fashionable

resort for diabetic and gouty patients; the waters contain bicarbonates and sulphates of lime, magnesia, and iron; the different springs vary somewhat, some containing more of certain constituents than others; traces of arsenic are said to be present.

It cannot be said that the specific effect of any of these waters has ever been demonstrated satisfactorily, but patients who go to these places find themselves able to spend the whole day in the open-air; their meals are served in gardens or on terraces; they get up early, live temperately, enjoy a very unwonted amount of sunshine, drink only light wines, in many places the growth of the neighbourhood, and take under medical advice draughts of, for the most part, innocuous waters. No doubt the waters at some of these places are not to be trifled with, notably those of Carlsbad, and are not to be recommended to weakly or nervous patients. To stand the Carlsbad cure a patient should possess a good margin of strength and stability, and many would do well enough at Neuenahr or Homburg whom a course at Carlsbad might injure.

Patients who are unable to visit these places may try the effect of the waters at home, but from what has been said above, divorced from their surroundings they do not promise much benefit. The waters of La Bourboule, Vichy, and Contrexéville may be used as table waters to mix with wine or lemon juice; and Carlsbad water or Carlsbad salt or the water of Châtel-Guyon may be employed as aperients when such remedies are needed.

EXERCISE AND FRESH AIR.—Although I have already expressed my opinion of the great importance of these for the maintenance of health in diabetes, it is desirable to emphasize it by a separate paragraph. Sedentary modes of life seem most favourable to the development of diabetes, while those who labour in the open-air rarely suffer. Open-air life must therefore be insisted upon, but the amount and nature of the exercise may vary. In particular we must enjoin abstinence from pursuits or exercises requiring strenuous exertion or involving great effort. In all cases the exercise should be regulated so as to avoid fatigue. The evil effects of over-exertion in precipitating fatal coma have been already commented upon and illustrated, but apart from such tragic results, excessive exercise may cause loss of strength and weight which is never regained.

BATHS.—Diabetic patients often derive great comfort from bathing. A hot-water bath is the simplest, and most suitable for severe cases. Fat diabetics may use the Turkish bath with benefit. The Russian or vapour bath is also valuable. This treatment is specially indicated where the skin is dry and irritable.

Massage has been strongly recommended by Finkler, as not only causing a general improvement in health and strength, but as leading to diminution of sugar, which in one case entirely disappeared. Aye has more recently published a case in which considerable benefit followed this mode of treatment, so that he was able to give up his dietetic regimen and discontinue the use of opium. The plan is worthy of adoption, but we must not expect too much from it.

DRUGS.—We may now pass to the important subject of the specific treatment of the disease by drugs. Two things are aimed at by their use—the limitation of the urinary secretion, and the diminution of the amount of sugar.

Of many remedies suggested there are four which claim the chief share of our attention. Opium is the oldest, and still retains the first place; next, its alkaloids, morphine and codeine; then salicylic acid or its salts; and lastly, salts of bromine.

The difficulty of carrying out strict comparative experiments with drugs is very great, because over and above the time and labour involved it is oftentimes impossible to secure the necessary conditions for their success, viz., that the other factors of the experiment shall remain undisturbed —diarrhœa, a severe attack of toothache (to which diabetics are very liable), inability to continue the same diet, and other accidents interfere with the course of the experiment, and oblige us to reject cases as untrustworthy upon which a good deal of time has been spent.

The following table shows the effect of *opium* as compared with diet alone and with other drugs. The other drugs used

ORDINARY DIET.			DIABETIC DIET.			WITH OTHER DRUGS.			WITH OPIUM.		
Total Urine.	Sp. gr.	Sugar p. c.	Total Urine.	Sp. gr.	Sugar p. c.	Total Urine.	Sp. gr.	Sugar p. c.	Total Urine.	Sp. gr.	Sugar p. c.
244	1040	10	200	1034	8	170	1030	8	176	1030	6·6

were arsenite of bromine, salicylate of sodium, bromide of potassium, lithia, codeine, salicin, boracic acid, and uranium nitrate.

The case was that of A. P., aged twenty-five, already quoted (Case 65).

This man took two grains of extract of opium three times a day, a much larger dose than usual.

The next case, E. H., aged twenty-seven, shows a more striking result, but the only drug with which opium was compared was salicylate of sodium.

ORDINARY DIET.			DIABETIC DIET.			SALICYLATE OF SODIUM.			OPIUM.		
Total Urine.	Sp. gr	Sugar p. c.	Total Urine.	Sp. gr.	Sugar p. c.	Total Urine.	Sp. gr.	Sugar p. c.	Total Urine.	Sp. gr.	Sugar p. c.
186	1042	5·8	158	1031	4·76	110	1038	4·76	58	1034	4·5

The dose was one grain of extract of opium twice daily.

Opium is especially valuable for the influence it appears to exert in diminishing the amount of urine. An opium pill often gives an undisturbed night to patients who without it have to rise frequently to pass water. Villemin recommends the combination of belladonna with opium. *Morphine* acts equally well, but *codeine*, when given even in much larger doses than are suggested by its principal advocates, is comparatively inert.

CASE 74.—*Diabetes Mellitus—cured by diet and opium.*

Henry H., aged fifty-seven, collier, attended as an out-patient on Jan. 4th, 1887, complaining of thirst and of passing a large quantity of water, seven pints daily. He was put on extract of opium (gr. j) three times a day, and anti-diabetic diet. By March 22nd the quantity of urine had fallen to two-and-a-half pints, sp. gr. 1015, and the sugar had disappeared. He was allowed to take modified diet, viz., bread and potatoes, and on April 19th the absence of sugar was confirmed.

CASE 75.—*Diabetes Mellitus—temporary disappearance of sugar under dietetic restrictions and opium.*

George E., aged sixty-one, attended as out-patient on Dec. 6th, 1887, complaining of thirst and of getting up a dozen times at night to make water. Quantity of urine five pints, pale, clear, sp. gr. 1027, contained a moderate quantity of sugar. Weight of patient 218 lbs. He had been ill two years. On anti-diabetic diet and extract of opium (gr. j) three times a day, by May 8th the quantity of water had fallen to three pints, of sp. gr. 1018, free from sugar. He then began to eat bread freely, and the sugar returned, though the quantity of urine remained low. Jambul and antipyrin were tried without effect on the sugar.

I have treated many cases with and without opium, and the strong impression left on my mind by these cases, is that in opium we possess the most valuable drug for the treatment of this disease, but I do not use opium in every case or continue it after it appears to have done its work.

Salicylate of sodium as an alkali may be of some service, for I am strongly in favour of the alkaline treatment of diabetes, but I have never observed it to produce any specific effect on the quantity of water or the amount of sugar, although Sympson has published a very good case of the disappearance of sugar in a boy of seventeen, under the use of this drug in ten-grain doses every four hours, combined with strict diet.

Arsenite of bromine, whether used pure or in the form of Clemens' solution* has never in my hands justified the praises it has received in some quarters; I have used it in many cases without being able to observe any specific effect. I have given it in doses of $\frac{1}{8}$ gr. of the pure drug, and up to ten minims of the solution. Another form in which arsenic may be given is that known as Martineau's specific.†

Bromide of potassium does not deserve the name of a specific, but is, in my opinion, the best routine remedy to employ in conjunction with the use of opium. It is suitably given in a mixture combined with a little bicarbonate of potassium and some bitter infusion, and very satisfactorily allays the nervous irritability so often present.

Teissier has found it very useful in the treatment of the diabetes of elderly women in doses of thirty to forty-five grains daily; but we know that this is a mild form of diabetes, with a natural tendency to amelioration or cure.

The relation of the pancreas to diabetes mellitus, and the success attending the employment of raw thyroid gland or extract in the treatment of myxœdema, naturally led to great hopes from *pancreatic remedies*. But Minkowski found that dogs rendered diabetic by extirpation of the pancreas were

* *Liquor Clementis.*—According to Hager its composition is as follows:—*Acidi Arseniosi, Potassii Carbonatis*, āā gr. jss. Place in a test tube and add five drops of distilled water, and warm so as to form a clear solution. Dilute this with distilled water till the quantity weighs 153 grains. Then add 6·2 grains (4 drops) of bromine and set aside for one day. The fluid is then ready for dispensing. A modified formula is frequently employed now.

† *Carbonate of Lithium*, 20 centigrammes (3 grains), added to a tablespoonful of the following solution:—*Arseniate of Sodium*, 0·20 centigramme ($\frac{1}{300}$ grain); *Distilled Water*, 500 centigrammes (80 minims); the mixture to be placed in an ordinary soda-water machine (Briet's apparatus), and this quantity to be used daily with and between meals, as a drink, alone or mixed with wine.

not benefited by being fed with fresh pancreas, or by the hypodermic injection of fresh pancreatic emulsion, and numerous clinical experiments with all sorts of preparations of the gland administered in the most varied way, have alike been fruitless. Lépine, following in the line of his theory of pancreatic diabetes as being dependent upon the absence of a glycolytic ferment, recommends a glycolytic ferment which he prepares by digesting five grammes of malt diastase in a litre of water to which one gramme of sulphuric acid is added, the mixture to be kept at from 35° to 38° C. (95° to 100·4° F.), for three hours; it is then neutralised with bicarbonate of soda. It should be made fresh every day, and this quantity (1 litre) is the daily dose. He reports three cases in which the quantity of sugar fell, under the use of this remedy.

Among other remedies recommended are *antipyrin* in 15 grain doses thrice daily (GERMAIN SÉE); *sulphide of calcium*, in doses of $\frac{1}{4}$ to $\frac{1}{2}$ grain, three or four times in twenty-four hours (CAULDWELL, DRAPER); *creasote*, 4 to 10 drops daily (VALENTINE); *phenacetin* and *exalgine* (DUJARDIN-BEAUMETZ); *camphor* (PEYRAUD); *iodoform* (MOLESCHOTT); *nitro-glycerine* (KENNEDY); *salicin*, in doses of from 2 to 18 grammes (30 to 270 grains) daily (DORNBLÜTH); *carbonate of soda*, $\frac{1}{2}$ oz. to 2 ozs. daily, with *citric acid* (STADELMANN); 5 to 6 ozs. daily of a 10 per cent. infusion of the bark of *syzygium jambolanum* (QUANJER); *sulpho-carbolate of soda*, 5 to 30 grains for a dose (MONCKTON); *pilocarpine* ($\frac{1}{20}$ grain), with 1 grain of sulphate of potash, three times daily (EAGER); *nitric* or *nitro-hydrochloric acid*, with tincture of *nux vomica* (WILKS); *cocaine* ($\frac{1}{4}$ grain), three times a day (OLIVER); *pepsin*, 10 grains three times a day (GARDNER); *jambul* (powdered bark of *eugenia jambolana*), in doses of 3 to 5 grains, thrice daily (KINGSBURY); *ouabaïn*, in doses of $\frac{1}{1000}$ of a grain three or four times a day (GEMMELL); *phosphorus*, in perles containing each $\frac{1}{50}$ of a grain, of which three and then six were taken daily (BALMANNO SQUIRE); *uranium nitrate*, up to 30 grains daily (WEST); *ergot*, the liquid extract ʒss three times a day (DOUGALL); *benzosol*, 4 to 5 grammes (60 to 75 grs.) daily (PIATKOWSKI); *strontium bromide* 30 grains daily (SOLIS COHEN); *permanganate of potash* and *maté* (MONIN); *piperazin* (HILDEBRANDT).

Jambul.—This drug was originally recommended by Banatvala of Madras, and spoken of in terms of highest praise. More recently Quanjer in Java has had an equally favourable

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experience of it. Both of these writers mention the syzygium jambolanum as the source. Kingsbury, who drew the attention of the profession in this country to its use by the recital of some successes he had met with, speaks of the plant as eugenia jambolana. On consulting Messrs. Christy, I am informed that these plants are the same.

In my observations the drug was administered in the form of Christy's jambul perles, or liquid extract prepared from freshly imported jambul seeds.

CASE 76.—A. J., aged eighteen :—

Diet.—Meat, greens, Bonthron's gluten bread, and one pint of milk. This was not changed throughout.

DOSE.	DURATION.	URINE.	SUGAR.	BODY WEIGHT.
Morphine—				
¼ grain thrice daily	7 days	85 oz.	9 per cent.	5 st. 4¾ lbs.
Jambul—				
6 perles daily	3 days	100 oz.	7·6 per cent.	
9 perles daily	6 days	100 oz.	6·8 per cent.	
12 perles daily	6 days	104 oz.	8 per cent.	5 st. 6½ lbs.
Ext. Opii—				
3 grains daily	7 days	76 oz.	5·4 per cent.	5 st. 10 lbs.

CASE 77.—W., aged thirty-three :—

Diet.—Meat, greens, Bonthron's gluten bread, potatoes, one pint of milk.

DOSE.	DURATION.	URINE.	SUGAR.	BODY WEIGHT.
Morphine—				
¼ grain daily	6 days	167 oz.	9 per cent.	8 st. 5½ lbs.
Jambul—				
6 perles daily	6 days	205 oz.	5·2 per cent.	8 st. 5¼ lbs.
9 perles daily	5 days	285 oz.	5·8 per cent.	
12 perles daily	4 days	394 oz.	7·6 per cent.	8 st. 3 lbs.
Ext. Opii—				
3 grains daily	7 days	200 oz.	6·6 per cent.	8 st. 8½ lbs.

In another case as many as thirty-six perles were given daily without effect, and a liquid extract also supplied by Messrs. Christy was given in several cases in doses gradually rising to 1½ ozs. daily.

It was tried in every case under treatment about the same time, and in no single instance was any distinct benefit

observed to follow its use. Minkowski found jambul absolutely useless in experimental pancreatic diabetes.

During the administration of *ouabaïn* for whooping-cough, sugar was observed to disappear from the urine of one of the cases on which it was tried (GEMMELL). Messrs. Christy kindly supplied me with a sample of *liq. ouabaïni* prepared by them, which I administered to several diabetics without observing any benefit. The dose was carried as high as nine drachms daily, beyond which I did not venture to go.

Ouabaïn is an alkaloid having the following composition :— $C_{30}H_{46}O_{12}$; it is obtained from the ouabaïs plant which is used as an arrow poison by the Somalis on the East Coast of Africa.

Phosphorus, which was recommended by Balmanno Squire because he had observed the sugar disappear during its use from the urine of an elderly man suffering from eczema, has had an extensive trial without any evidence being obtained that it possesses the power to control any of the important symptoms of diabetes, and exactly the same may be said of cocaine, which was recommended by Oliver on theoretical grounds.

Benzosol, 15 or 20 grains three or four times a day, is being largely used at present in Germany, sometimes with good results.

Grube has drawn attention to the improvement in the general health which followed the use of a heaped up teaspoonful of powdered egg-shell, by two patients. The remedy is a bit of folk-lore, but Grube thinks it fulfils the indication afforded by the great loss of lime from the body, and suggests the use of a teaspoonful daily of a powder consisting of 93 parts of carbonate of lime and 7 parts of phosphate of lime. It has no influence on the glycosuria.

TREATMENT OF SYMPTOMS.—*Neuralgia.*—In many instances, as in cases quoted, diabetic neuralgia ceases when the disease is checked by general treatment. But to afford relief we may give antipyrin, 15 or 20 grains for a dose, or exalgine, 3 to 4 grains for a dose, or opium or morphia, by the mouth or hypodermically. The following ointment may be used locally: ℞ *Menthol*, gr. xv; *Cocaine*, gr. v; *Chloral Hydratis*, gr. iij; *Vaseline*, ʒj; *Fiat Unguentum.* Sig.—To be rubbed gently over the seat of pain.

Thirst depends on the great drain of water from the body, and the rational treatment of it is to lessen the polyuria. In

the meantime no good purpose is served by placing restrictions on the quantity of fluid to be drunk, as this can only augment the patient's suffering without any benefit. Sucking ice, or the use of lemon or bitartrate of potash water as a drink, may check it. With the object of promoting a flow of saliva and so relieving the dryness of the mouth, hypodermic injections of pilocarpine (grain $\frac{1}{20}$ to $\frac{1}{8}$) have been frequently used, and with good results. McAvoy recommends for the same purpose 5 minim doses of glycerinum acidi carbolici. Constipation appears in some cases to increase thirst.

A subordinate but nevertheless highly important detail of treatment is the regulation of the bowels. All, or almost all, diabetics are *constipated*, whatever they may say. I have seldom made a post-mortem examination of a subject of this disease without finding the colon stuffed with hardened masses of fæces. Therefore, it is usually necessary to give a purgative twice a week. We may use any of the favourite or fashionable remedies, avoiding only such preparations as contain sugar, but one of the most certain is Rubinat water.

The *œdema* of diabetes generally disappears very rapidly on rest in bed and appropriate general treatment. Dickinson thinks large doses of perchloride of iron (30 to 40 minims of the tincture three or four times a day) act as a specific. Massage should be tried in all obstinate cases.

Pruritus.—This may be treated by careful cleansing with a sponge dipped in some antiseptic fluid after micturition. Lawson Tait speaks very favourably of the use of a lotion containing hyposulphite of soda, an ounce to a quart of water, and of an ointment containing 10 grains of sulphuret of potassium to the ounce, combined with the use of opium. A warm freshly-made saturated solution of boracic acid may be used with confidence that it will give relief, and after carefully drying the parts, zinc ointment should be applied freely, but it is right to say that the condition, possibly from want of care on the part of the patient, is sometimes very intractable.

Routh recommends the following remedies:—Put a teaspoonful of borax into a pint bottle of hot water, add 5 drops of oil of peppermint and shake well. Bathe the affected parts freely with a soft sponge. If rawness or eczema is present, apply olive oil to which iodoform has been added in the proportion of 5 grains to the ounce.

Sweating.—This is a rare affection, and according to Schmitz, is a favourable symptom, so that it may not be always desir-

able to check it. But where this is the case I have found that Dover's powder, taken as a substitute for the opium preparation previously in use, has proved very useful.

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CHAPTER XXII.

DIABETES INSIPIDUS.

IN spite of the discovery of Willis, in 1670, of the presence of sugar in the urine in certain cases of diabetes, it was not till the end of the eighteenth century that the formal distinction into diabetes mellitus (verus) and diabetes insipidus (spurius) was made by Cullen.

Diabetes insipidus, according to Senator, is the name applied to every case of chronic morbidly increased secretion of urine, free from sugar, which is caused by no profound structural alteration of the kidneys, and which constitutes either the sole or at least the most prominent and primary morbid phenomenon. According to this definition it is the polyuria which causes the thirst, but there are cases in which the thirst is primary, so that it is preferable to define the disease simply as characterised by the two symptoms, *thirst, and polyuria, with absence of glycosuria.* Synonyms for this condition are *polyuria, polydipsia, hydruria*, etc.

ETIOLOGY.

Bernard caused simple polyuria by puncture of the floor of the fourth ventricle near the spot injury of which is followed by glycosuria. Eckhard produced similar results in rabbits, by injuring the posterior lobe of the vermiform process of the cerebellum. Peyrani induced the condition by electrical stimulation of the cervical sympathetic; and it is said to follow section of the splanchnic nerves.

Predisposing Causes.—The *age* at which the disease occurs is illustrated in the following table:—

AGE.	ROBERTS.	STRAUSS.	VAN DER HEIJDEN.
Under 5 yrs.	7	9	2
5—10	15	12	5
10—20	13	57	19
20—30	16		23
30—40	—		19
40—50	15		9
50—60	—	7	6
60—70	4	—	4
	70	85	87

This shows that the greatest frequency is during adolescence, early manhood and middle life, infancy and old age being comparatively exempt. The male sex seems decidedly more liable than the female in the proportion of nearly three to one :—

NAME.	MALES.	FEMALES.
Roberts	55	22
Van der Heijden	71	25
	126	47

The influence of *heredity* is well known. Weil has published a very remarkable history of a family in which no less than twenty individuals out of a total of ninety-one, in four generations, were attacked by the disease. Males and females were attacked in equal proportions, and no age appeared exempt. There was no evidence of scrofula or tubercle in the family; all the males were well developed and had performed their military service. It seemed to have no influence on their vitality, the diabetic ancestor having lived to be eighty-three, his daughter to seventy-four, and two living members, also affected, had attained the ages of sixty-seven and seventy-six respectively.

In Lacombe's case, a mother, her four children, and her brother and his children were all affected.

It has been supposed that the *tubercular* diathesis is a predisposing cause, and although in Weil's family, just quoted, there was no evidence of such a taint, R. H. Clay has recorded the cases of three children, two brothers and a sister, suffering from diabetes insipidus, in whose family four other children had died of consumption.

Syphilis is undoubtedly a cause, but in this case the effect is generally due to the formation of a gumma in the brain.

Gout is probably to be reckoned as a predisposing factor, and so is *insanity*.

Among the *exciting causes*, severe *contusions* in various parts, but particularly the head, occupy a well-defined place. One of Matthews Duncan's cases was apparently caused by a blow of great severity on the back of the head. Flatten has reported a case in which a blow from the trunk of a tree on

the left side of the neck and occipital region, was followed in seven days by great thirst and polyuria, accompanied by complete paralysis of the left external rectus oculi muscle, and a slight paresis of the corresponding muscle on the right side. He thinks the blow caused a circumscribed hæmorrhagic softening on the level of the point of exit of the abducens nerves in the hindermost part of the pons or the anterior part of the medulla. Drummond, of Newcastle, has described a case in which the disease came on suddenly in a man who had been roughly throttled by a fellow workman, and in the discussion which followed Oliver mentioned the case of a man who fell into a dock and was rendered unconscious for ten or twelve days; on recovering consciousness he drank greedily, and from that moment polydipsia and polyuria existed. A case came under my observation several years ago, where a fall from a train in motion was followed by temporary glycosuria and by polyuria which has persisted.

Nothnägel recorded the case of a man aged thirty-four, who was kicked in the left side of the abdomen and fell with the back of his head on a hard floor. He suffered from pain with a sense of compression in the occiput, and his pupils were much contracted. Soon after, he was seized with thirst and passed a large quantity of water. These symptoms gradually disappeared, and eighteen days after his accident he was discharged cured.

The influence of *pregnancy* is also not to be doubted, but the condition appears to be temporary. Thus in Hughes Bennett's case the disease came on at the fifth month and disappeared two days after delivery; in Matthews Duncan's case it disappeared a month after delivery, and in Esterle's the disease appeared in two successive pregnancies, but disappeared in the interval. Westphal has published a case which he attributed to the loss of blood at the confinement. Senator has recorded a case which after lasting several years *disappeared* on the supervention of pregnancy.

Possibly in close alliance with the last-named cause, in their mode of origin, are those cases in which *abdominal tumours* have been associated with this disease. Ralfe had met with it in two cases of *aortic aneurysm*, and Haughton in a case of *uterine fibroid*, with enlargement of the mesenteric glands and fæcal accumulation. Ralfe believed the aneurysms pressed upon the vagus.

Somewhat allied, too, is the case described by Küster, which followed the incision and drainage of a *pancreatic cyst*, but there may have been injury to the splanchnic nerves or vagi.

Among other exciting causes are exposure to *cold* and drinking cold fluids when heated, *infective diseases*, *muscular effort*, exposure to a *hot sun*, and *mental emotion*.

As illustrations of the effect of *muscular effort* may be quoted Frank's case of a boy who strained himself by pushing the wheel of a cart which was sunk in the mud; and Jarrold's of a girl who slipped, but saved herself from falling by a very great exertion.

Jacobi has recorded a case which was cured by the removal of a tænia medio-canellata; but in a case of Lunin's, removal of the worm was not followed by any benefit to the specific symptoms.

Acute alcoholic intoxication is stated by Dickinson to be an indubitable exciting cause; in his own words "a person gets what is vulgarly called dead drunk"; on regaining consciousness he is polyuric and so remains.

Finally, lesions of various parts of the nervous system are direct exciting causes of the disease, but these are better described under the heading of morbid anatomy.

MORBID ANATOMY.

Nervous System.—Various lesions of the *brain* have been observed, such as fracture of the base of the skull, with contusion of the anterior lobes; yellow softening, inflammation and degeneration in the floor of the fourth ventricle. Tumours, tubercle, glio-sarcoma, gummata, and exostoses in various positions; carcinoma of the pineal gland. Lesions have also been found in the semi-lunar ganglia and splanchnic nerves. The ganglia showed the atrophy of nerve cells associated with increase of connective tissue and dilatation of vessels, which is seen in so many diseases. The nerves showed fatty degeneration of their axis cylinders, with granular degeneration and dilatation of the vessels of the neurilemma (SCHAPIRO).

The Blood.—According to Strauss, the solids of the blood are increased:—

	First Observation.	Second Observation.
Water	77·79 per cent.	77·937 per cent.
Solids	22·21 per cent.	22·063 per cent.
	100·00	100·000

The solids in the second case consisted of:—

Fibrin : - - - - - -	0·467 per cent.
Hæmoglobin - - - - -	11·72 per cent.
Other Albuminoids - - - - -	7·441 per cent.
Extractives - - - - - -	1·301 per cent.
Ash - - - - - - - -	1·134 per cent.

The serum contained:—

Water - - - - - -	88·712 per cent.
Albumen - - - - - -	9·062 per cent.
Extractives - - - - -	1·012 per cent.
Ash - - - - - - -	1·214 per cent.

Alimentary System.—The mucous membrane of the large intestine may be ulcerated and ecchymosed (SCHAPIRO), or there may be tubercular ulceration (ROBERTS). Dickinson has observed cancer of the liver in one instance.

Respiratory System.—Where, as has several times happened, the disease is connected with tubercle, there may be more or less extensive pulmonary phthisis. Lobular pneumonia was present in one case (NEUFFER). As a rule the lungs are normal.

Urinary System.—The kidneys appear normal or may be congested, the Malpighian bodies especially appearing as well marked hyperæmic points.

Secondary changes in the kidneys are not uncommon. Thus Neuffer describes a case in which the renal tubules were dilated, some being stripped of their epithelium, others stuffed with fatty *débris*; Beale observed similar changes, together with increase of the peri-vascular connective tissue. In some cases the kidneys are sacculated, the cavities containing urine or pus, and the bladder and ureters are also thickened and dilated (see Case 80, p. 384).

PATHOLOGY.—There can be little doubt that the disease is a neurosis which depends upon changes in the nerve centres, or upon peripheral irritation acting through those centres. The channel for the transmission of the morbid influence appears to be the vagus nerve, and the mechanism consists in relaxing the tonus of the renal arterioles and permitting a very free afflux of blood to the Malpighian bodies.

SYMPTOMS, AND CLINICAL HISTORY.

As has been already stated, the cardinal symptoms are thirst and polyuria. In certain cases thirst is the first symptom noticed; in others, and perhaps in the majority, polyuria is the primary affection.

The following case illustrates very well the type in which thirst precedes polyuria :—

CASE 78.—*Diabetes Insipidus—thirst—polyuria—gouty history—improvement.*

John P., forty-nine, came as an out-patient on April 10th, 1883, complaining of thirst and passing a large quantity of water. He said that his illness began quite suddenly six years before. He was out for a walk one Sunday when "a great thirst came on him, so that at every house or brook he came to he must be drinking." He was in perfectly good health, and had not met with any accident. He had worked as a stamper in Birmingham, and had always enjoyed good health. The only illness he could recall was "stoppage of the water" eighteen years before, but he soon recovered. He was a married man, but had no children living. Two were born dead and his wife had had several miscarriages, but he could give no history of syphilis, sore throat, or skin eruption, though he admitted having had gonorrhœa when he was nineteen. He had no knowledge of any similar case in the family. He had had gout several times. He was a well-nourished man; there was a depressed scar over the right frontal eminence, which was caused by a fall in early childhood before he could remember. He weighed 12 st. 7 lbs. His tongue was furred posteriorly, and he suffered from pain and wind, after food. His bowels were regular; liver and spleen normal. He complained of severe cough and spit, and shortness of breath, but he had no palpitation or œdema of feet; his heart and lungs appeared normal. Pulse 120. He said that he passed a chamber-pot full of water in the night and more in the day. The urine was clear, pale yellow, sp. gr. 1001, faintly acid, no albumen or sugar. Ophthalmoscopic signs negative. He had no headache, giddiness, or vomiting. He was treated by colchicum, carbonate of magnesia, and sulphate of magnesia, and under these remedies his polyuria and thirst greatly diminished.

As will have been noted, this disease does not necessarily involve weakness or loss of flesh, but is consistent with good general health. In some cases, there is wasting and evident ill-health, in others obesity (VOSS).

The flow of saliva may be greatly increased (KUELZ), and there are often pains in the back and loins. The bowels are generally confined. The temperature of the body is normal, in some cases it is sub-normal. When it comes on early in life it affects the growth of the individual. The following is a good example of this type of case :—

CASE 79.—*Diabetes Insipidus—neurotic family history—stunted growth—polydipsia.*

Frederick S., sixteen, jeweller, was admitted into the General Hospital on June 19th, 1890, complaining of thirst and of passing large quantities of water.

Family History.—Father died aged thirty, from "diseased bowels." Mother alive, aged forty-two, had been an inmate of a lunatic asylum for three years. She suffered from fits before becoming insane. Two brothers living—one died in infancy. No history of phthisis or diabetes.

Previous History.—Patient was always weak. He had measles at six years of age. Ever since his infancy he had passed water in large quantities, and had suffered from thirst. For the last three years he had been in the habit of drinking quite a quart of water during each night. His appetite had never been excessive.

Present Condition.—Patient was fairly well nourished, very small for his age; weight 4 st. 6 lbs.; height 4 ft. 7¾ in. No jaundice, œdema, or special dryness of skin. He seemed very lively and intelligent. Pulse 80; Resp., 16; Temp., 98·5°

Alimentary System.—There was a red line along the margin of the gums. Tongue moist and furred. Appetite poor. Thirst marked; he drank 6½ pints of fluid yesterday, and one pint in the night. No pain after food, or vomiting. Bowels rather confined. Liver dulness in V.M.L., 3 in. Splenic dulness in M.A.L., 1½ in.

Circulatory System.—There were some dyspnœa and palpitation on exertion; cardiac impulse obscure, in 5th I.S., in V.M.L. Cardiac dulness was bounded above by the 3rd C.C. to the right by the right edge of the sternum, and to the left by the V.M.L. Heart sounds rather feeble; pulmonary second sound reduplicated; no murmur. Pulse regular, fairly strong, easily compressed.

Respiratory System.—No cough. There were some dilated veins over the upper part of the front of the thorax. Sternum rather convex. Vocal fremitus feeble; percussion note resonant; breath sounds vesicular; vocal resonance normal; no adventitious sounds.

Urinary System.—Micturition frequent; usually about three times in the night. No scalding or pain. Urine 104 ozs., sp. gr. 1002, neutral, pale opalescent straw colour; white deposit consisting of bacteria, mucus, leucocytes and triple phosphates; urea 0·65 per cent.; a haze of albumen, no sugar or blood.

Analysis of another specimen showed total solids to be only 0·66 per cent. These were made up as follows:—

Organic substances—		
Urea - - -	0·324	
Albumen and mucus	0·040	= 0·364 per cent.
Inorganic substances—		
Chlorides - -	0·023	
Sulphates - -	0·044	
Soluble phosphates -	0·060	
Insoluble phosphates	0·020	
Magnesia, Lime, Soda, and Potash - -	0·149	= 0·296 per cent.

There was a disposition for his temperature to be subnormal, ranging from 97·5 to 98°. He gained no weight while under treatment, nor was the urine affected by the drugs employed, viz., a mixture of dilute hydrochloric acid with a bitter infusion, given well diluted with water as a drink, and 3 grains of ergotin daily, in the form of pills, containing each 1 grain.

The following table shows the quantity of fluid ingested and the quantity of urine passed in corresponding periods of twenty-four hours, during his stay in hospital.

DATE.	URINE IN OUNCES.	FLUID INGESTED IN OUNCES.
June 22	104	130
„ 23	110	120
„ 24	126	100
„ 25	106	100
„ 26	116	120
„ 27	108	120
„ 28	122	140
„ 29	118	130
„ 30	136	150
July 1	160	150
„ 2	140	140
„ 3	120	130
„ 4	128	110
„ 5	130	110
„ 6	120	130
„ 7	122	110
„ 8	128	120
„ 9	100	110

These patients suffer a good deal from dryness of the skin, and dry mouth and fauces. There may be a good deal of gastric disturbance, especially when the kidneys are becoming disorganised. According to Lowinsky, boils, originating in inflammation of the sweat glands, may occur. The bladder may become very irritable, and œdema of the feet may supervene in the later stages.

Great intolerance of alcohol has been observed, which is the more remarkable as it must be excreted very rapidly, while Trousseau has recorded a case in which great tolerance existed, the patient being able to drink twenty litres of wine and a litre of brandy at a sitting.

Hunger may be present in a very marked degree, and Trousseau speaks of these patients as the terror of the keepers of restaurants *à prix fixe*.

The *Urine* is always greatly increased; it may be faintly acid, alkaline, or neutral; it is always of low specific gravity, and as a rule free from albumen. It contains no glucose, though cases in which diabetes insipidus appears to alternate with diabetes mellitus have been observed. Inosite, or muscle

sugar, has been frequently found to be present (SCHULZEN, STRAUSS), but it is not constant. It is detected by evaporating the urine to dryness, then moistening with ammonia and a solution of calcium chloride, and evaporating again. If inosite is present a ruby red colour makes its appearance (SCHERER).

The polyuria is occasionally intermittent (FAGGE).

The urea is greatly increased until the kidneys become disorganised, when it diminishes to below the normal amount; under these circumstances pus or albumen may be present. The uric acid is probably normal; kreatin and kreatinin are said to be diminished (STRAUSS, PRIBRAM); hippuric acid is present (BOUCHARDAT); the chlorides are increased (SENATOR); and so are the phosphates.

CASE 80.—*Diabetes insipidus—with sacculated kidneys—uræmia.*

Alfred W., aged 26, a sieve-maker, was admitted into Hospital on September 12th, 1894, complaining of intense thirst, frequent micturition, and the passage of a large quantity of urine. This was the third occasion on which he had been an inmate of our wards for practically the same symptoms. He had suffered from thirst all his life, but he believed he had gradually got worse. For the last ten years he had been subject to attacks of pain in the abdomen, and when in hospital for the first time, four years ago, there was some tenderness on palpation in the right lumbar region. On the second occasion, tenderness in the abdomen was noted "over both kidneys, but no marked enlargement of either"; this was in 1891. He contracted gonorrhœa about four years before his final admission, probably before he came to the hospital at all, and he has since suffered from a persistent gleet. His family history reveals no instance of a similar condition nor any evidence of diathetic disease, except in the person of an uncle, who suffers from gout. The patient was a slenderly-developed, badly-nourished man, looking younger than his age; he weighed 8 st., and as in 1890 he weighed 8 st. 3 lbs., and in 1891 7st. 11 lbs., we may take it that he has been about the same weight for some years, although he stated on admission that he had recently been losing flesh. His skin was very dry, and his face flushed; T. 97·5°, P. 78, R. 16. His appetite was very poor, but his thirst was constant, disturbing his sleep. His tongue was furred and furrowed. He vomited nearly every morning, the vomited matter consisting of watery mucus for the most part. He had lived in a beershop and had all his life been accustomed to drink large quantities of beer to relieve his thirst. His abdomen was tender, especially over the left kidney; liver and spleen not enlarged; bowels confined. He suffered from pain at the præcordia, with frequent attacks of dyspnœa, but the heart sounds, though weak, were pure, and this organ was not obviously altered in size; lungs normal. He stammered in his speech, and had some complaint of numbness in his fingers and toes; but in other respects his nervous system presented no anomaly. The urine on each occasion of his stay in hospital measured between five and six pints; but he told us that when he was going about it was more, and his thirst was greater; its sp. gr. was about 1010, and its reaction was gener-

ally alkaline. This time it contained a very little albumen due to pus; there was no sugar; the urea was diminished, being little over 200 grains in twenty-four hours; no casts were ever found, but some pus corpuscles were constantly deposited.

Analysis of the Urine.—Total urine 178 oz.; Sp. gr. 1005; Total solids 0·9; Organic matter 0·596; Urea 0·55; Albumen traces; Sugar none; Inosite none; Inorganic matter 0·304; Chlorides 0·0230; Phosphates 0·0446; Sulphates 0·0782; Lime and magnesia 0·0250; Potash and soda 0·1332; Water 99·1.

He was treated, mainly for his stomach symptoms, by light diet, chiefly milk, bismuth and alkalies, and saline aperients. At first he improved, but in a few days he began to complain very bitterly of pains, neuralgic in character, in his legs; these were not relieved by salicylate of soda. On the 26th he was given a hypodermic injection of three minims of the Pharmacopœial hypodermic solution of morphia. After this he slept heavily all through the 27th and 28th, dying on the 29th of September. During this time he could be roused and answered sensibly, but when left alone he fell asleep again. He passed very little urine during this semi-comatose period. The *post mortem* examination was made on the 29th. The only noteworthy changes were some œdema of the lungs, slight hypertrophy of the left ventricle of the heart, a certain amount of enlargement and fatty change in the liver, but the kidneys require detailed description. Both these organs were in a state of hydronephrosis and they have been mounted for permanent preservation.

The *right* kidney presented a large cyst which bulged forwards under the peritoneum. On removing the organ, this cyst was found to be the greatly dilated renal pelvis. From the cortex to the hilum it measured three inches, and its length was the same. On section, the pyramids and cortex were much atrophied; the capsule was partially adherent; the ureter, which was much dilated, opened from the most depending part of the pelvis, and was not obstructed. The *left* kidney was small and its pelvis was dilated, though not to the same extent; it contained a concretion about the size of a hemp-seed. The ureter was also somewhat dilated, but not obstructed. The cortex was atrophied, and the capsule adherent. The weight of the two kidneys taken together was twelve ounces.

The bladder was enlarged and its walls thickened, but the orifices of the ureters and their lumina were quite patent. There was no prostatic disease or urethral stricture. I may add that the brain looked anæmic, but otherwise appeared normal, and that the medulla oblongata, examined microscopically, showed no morbid change.

It is well known that in this disease the excretion of urea is generally greater than normal, and may be enormously in excess. But in this case the amount of urea excreted daily was very little over 200 grains—a figure which, even on milk diet, is dangerously below the normal for an adult person. When he was in hospital in 1891 he excreted 480 grains of urea, so at that time he evidently possessed an adequate amount of healthy kidney substance.

We must therefore watch the urea excretion in all cases of

diabetes insipidus, and be on our guard against a fatal uræmic termination whenever this becomes persistently reduced below the physiological proportion, although this varies at different ages. Dr. Ralfe gave the following table:—

At 5 years	...	...	...	180 grains.
12 „	...	. .	...	320 „
21 „	. .	...	...	535 „
40 „	...	...	...	555 „

But I am accustomed to teach that these figures are too high for a patient in bed on milk diet. I believe the case is safe so long as the daily amount exceeds 300 grains.

Intercurrent infective diseases usually produce a diminution in the quantity of urine. This has been observed in small-pox (LACOMBE, CHARCOT, KUELZ), typhus (PRIBRAM), pleurisy (DESGRANGES), acute rheumatism (ROBERTS), pneumonia and erysipelas (SENATOR). But Dickinson has recorded a case in which an attack of scarlatina was attended by no diminution.

Affections of the *eye* do not form any part of the proper symptoms of this disease. Cataract is rare, and such conditions as double optic neuritis, atrophy of the optic nerve (GOWERS), retinal hæmorrhages (GALEZOWSKI), and staphyloma posticum (LAYCOCK), are either the consequences of some cerebral lesion, or accidental coincidences. The knee jerks may be exaggerated apart from cases following injury.

PROGNOSIS.—The *duration* of the disease is very indefinite, as it may exist the whole of a long lifetime, and does not appear to have any essential tendency to cause death.

Many instances of spontaneous cure have been recorded; thus a case that had existed eighteen years was cured by an attack of acute rheumatism, another by a pleurisy treated by blistering, and one already alluded to, by the removal of a tapeworm. A little patient, seen by me, was apparently cured by an attack of measles. Brunton has recorded a number of cases among European children in India, attributed to exposure to the sun, which all got well in a few weeks or months. Garnerus has recorded the case of a child who soon after birth suffered from polyuria with progressive emaciation, and during the second month sugar appeared in its urine. This disappeared later on, but the polyuria did not improve till the child was fed on milk from which the sugar was removed by fermentation, sweetened with glycerine and mannite and diluted with boiled water. After three months of this diet

ordinary milk was given it without any relapse following, and the child remained well.

The prognosis as to life is not unfavourable, as has been already shown in Weil's cases. The cause must determine this to some extent; obviously if there is reason to believe in disease of the central nervous system, the prognosis must depend on the curability of this condition. Where there is a history of syphilis a cure may be hoped for. We have seen that after injuries the condition may be temporary, and in pregnancy it terminates as a rule, at or soon after delivery. While the disease may exist for years without apparent alteration of health, when kidney changes set in, the patient eventually dies with symptoms of chronic uræmic poisoning; therefore evidences of renal affection, and especially diminution of urea, must be regarded as unfavourable.

TREATMENT.—In the majority of chronic idiopathic cases drugs are of little use. Where there is a syphilitic history mercury and iodide of potassium should have a prolonged trial.

One of the most highly recommended remedies is valerian, given either in the form of extract, in drachm doses, or valerianate of zinc, up to 15 grains, three times daily.

Ergot, in the form of the liquid extract, 10 to 30 minims, three times a day, or ergotin, in doses of 1, 2 or 3 grains, three times a day, have also been successful.

Eichhorst has cured a case with tincture of the acetate of iron, and another with 5 grammes (75 grains) of antipyrin, daily. The latter drug has been also successful in the hands of Laplane, Zenner, and Opitz.

Galvanisation applied to the nape of the neck (ALTHAUS, CLUBBE) has been strongly recommended.

Voniovitch has cured a case by ½ gramme doses of antipyrin, eight to twelve times daily. Clarke has reported considerable improvement after feeding with fresh supra-renal glands. Kennedy has urged the use of nitric or nitro-muriatic acid in doses of from 1 to 5 drachms daily. Libby has employed with advantage spirits of turpentine, 15 to 20 drops, three times a day. Murrell observed benefit in a traumatic case from a combination of ergot with belladonna, and Brunton used belladonna in all his successful cases. Roberts recommends a blister to the pit of the stomach.

It is useless and unnecessarily cruel to attempt to limit the quantity of fluid drunk. The dryness of the mouth may be

relieved by pilocarpin, or by sucking ice, or lemon, or glycerine lozenges. Opium or morphia may be tried to diminish the polyuria, but obviously the general condition of the patient must be our guide as to the extent to which we should push active treatment. While the general hygienic surroundings of the patient should be as satisfactory as they can be made, there is no reason to make him more of an invalid than he need be, and his diet, while wholesome and sufficient, should not be restricted.

The dryness of the skin may be relieved by frequent steam or hot water baths, and there is some advantage in anointing the skin after the bath with olive oil, scented by the addition of a few drops of rosemary or bergamot.

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SECTION IV.

MISCELLANEOUS RENAL DISEASES.

CHAPTER XXIII.

STONE IN THE KIDNEY.

STONE in the kidney, or renal calculus, is a condition attended by very varying indications. It may cause any degree of *pain* in the region of the kidney, from a dull aching to an intense agony which tries the strongest man; there may be *blood* or *pus* in the urine or *albumen* only, or nothing abnormal; the urine may be *increased* in quantity and frequency, or diminished or totally *suppressed*; and, finally, each or all of these symptoms may be present when the kidneys are quite free from stone.

This disease is very common in most parts of England, occurring at all ages and in both sexes, though more usually after middle age and in males. It is most often associated with a personal or family tendency to gout, and the most usual forms of calculi are composed of *uric acid* or *oxalate of lime*; more rarely we meet with stones formed mainly of phosphate of lime, generally with an organic nucleus, or of cystin, or of old and altered blood clot (MARTIN).

Phosphatic concretions may form around any foreign body lodged in the kidney; for example, on a nucleus of uric acid or oxalate of lime, or on a sewing needle (KENDAL FRANKS), or on a bristle (STEVEN). Such phosphatic stones are usually associated with suppuration in the kidney and are probably always dependent upon decomposition of the urine. Cystin calculi are always associated with the presence of cystin crystals in the urine, which can be easily recognised by their hexagonal shape. (*See page* 195.) Recent researches point to the possibility that cystin is in some way dependent upon abnormal putrefaction of the intestinal contents.

We know very little respecting the conditions under which blood clots become so altered and hardened as to form calculi, but they originate without doubt in hæmorrhage resulting from some injury to the kidney substance, such as might be inflicted by a blow or a crush.

Stone is particularly frequent in England in Norfolk and Suffolk; in Scotland in Fife and Aberdeenshire; while Hereford, Dorset and Durham are singularly free. Plowright has sought to establish a relation between the prevalence of stone and a low mean annual rainfall, but Durham is an exception to this rule. Cider drinking is supposed by some to be a preventive of stone, but it probably acts only by taking the place of beer which favours the uric acid diathesis. Hard drinking water is a factor in the production of stone; or at least there has been a very sensible diminution of the disease in South Staffordshire since the surface wells were closed and softer tap water introduced. Both uric acid and oxalate of lime calculi appear to be dependent upon the uric acid diathesis, perhaps in different degrees, and under certain not understood variations of the conditions, as the same person may at different times pass both kinds of stone.

The formation of a stone in the kidney may be due to abnormal positions of the organ, such as floating kidney or congenital displacement.

Calculi, others than those formed from blood clot, are composed of minute crystals or particles united by an organic cement substance, and increase in size until they may form a complete cast of the cavity in which they lie. They may be present and even grow to an extreme size, without giving rise to any subjective symptoms, though the kidney atrophies, until it forms merely a capsule of fibrous tissue or more rarely of true fat (RICKARDS). In other cases the stone passes into the bladder, and perhaps out from the urethra without pain. More commonly, it gives rise to pain and other troubles while in the kidney or during its passage into the bladder. A stone resting in the kidney may cause (1,) pain, (2,) hæmorrhage, and (3,) inflammation. The *pain* is usually referred to the loin, and there is often tenderness just outside the edge of the erector spinæ muscle. It is a dull aching pain, which radiates round the hip or towards the inner side of the thigh; sometimes down the leg, or to the front of the abdomen or into the hypogastrium. It has been mistaken for lumbago, sciatica, the gastric crisis of tabes, intestinal colic, or even labour, and

may be attended by persistent vomiting. The pain may be constant or intermittent; and in the latter case may be brought on by prolonged walking or standing; on the other hand it is usually relieved by rest, especially rest in bed, although in some instances it is worst at night (JACOBSON).

Sooner or later as a rule *hæmorrhage* occurs, generally moderate in amount, but enough to make the urine bloody and not merely smoky. Under the microscope the blood discs are usually seen to be accompanied by pear-shaped epithelial cells, pus cells and crystals, the last being generally of the same nature as the stone. There may also be a few hyaline casts, but no renal blood casts, as the blood comes from the renal pelvis and not from the substance of the kidney. Cylindrical blood-casts of the ureter, half-an-inch to an inch in length, are occasionally found in the urine.

More or less *inflammation* always attends the prolonged stay of a calculus in the kidney. This may reveal itself by great tenderness in the loin, indicating inflammation of the perinephric connective tissue, and may go on to the formation of perinephric abscess; or pus in quantity may appear in the urine from pyelitis or suppurative inflammation of the lining membrane of the renal pelvis; or suppurative interstitial inflammation, with the formation of abscesses of various size, may attack the kidney substance itself. The formation of abscesses may be attended by all the phenomena of septic fever—rigors, high temperature and sweating; while true pyæmia may develop with secondary abscesses in other organs. In addition there may be irritation of the skin, particularly in the epigastrium, urticaria, jaundice, or herpes zoster. If both the kidneys are affected uræmic symptoms appear, and occasionally when one kidney was found *post mortem* to be fairly healthy, there has been complete suppression of urine from reflex inhibition (GODLEE). When a perinephric abscess has formed, it causes pain, tenderness and swelling of the part; there may be bulging between the last rib and the crest of the ilium; or a tumour can be felt in the hypochondrium. If not opened such an abscess usually bursts externally, leaving a sinus through which pus is discharged. But when the stone becomes engaged in the ureter on its way to the bladder, it causes a very striking group of symptoms called *renal colic*, viz., (1,) pain, (2,) shivering, (3,) vomiting and diarrhœa, (4,) hæma-

turia, and (5,) suppression of urine; but all of these are not present in every case.

As already stated, a stone may pass into the bladder unnoticed and without pain, but as a rule this process is one of the most intense suffering; so much so that patients look back upon such an attack with horror. The immediate cause is often some unusual exertion or strain, jolting in a cart over a rough road, etc. One of my friends was getting into his carriage when the horse moved on, and he was thrown on to the back seat so as to give himself, as he thought, a twist in his loins. Pain came on at once, and in the course of the night he passed a stone. A young man who was the subject of cystin calculi brought on an attack by carrying his uncle in boyish fun upon his back. The pain is most excruciating; it starts from the kidney and shoots downwards and forwards to the groin; it is often accompanied by retraction of the testicle on the same side. In his agony the patient rolls about, clutching at the bed-clothes, and cannot restrain himself from groaning or shouting. It is said to have given rise to all the symptoms of labour (SALZMANN). At the beginning there is often *shivering*, and as the attack proceeds the body may be covered with *sweat.*

Vomiting is common, *diarrhœa* may occur, and there may be *hæmorrhage* from the rectum.

Hæmaturia is constant, except when the ureter is completely blocked.

There is great *frequency of micturition* from reflex excitement of the bladder, so that any blood voided is bright coloured. In most cases the attack terminates after a few hours by the passage of the stone into the bladder, whence it is usually voided with the urine. But it may block the urethra and require to be extracted, or remain in the bladder, increase in size, and require removal by crushing or cutting, or it may stick in the ureter and cause complete or incomplete obstruction of that duct, or, lastly, it may fall back into the pelvis of the kidney.

In the first and last cases when the attack is ended some tenderness may remain, but the patient soon resumes his ordinary mode of life. When the stone remains in the bladder it may not give much trouble for some time, and then develops a new group of symptoms which do not form part of my subject. If the calculus becomes impacted in the ureter it obstructs the outflow of the urine, which continues to

be secreted until the pressure within the tubules is equal to the blood pressure, when it of necessity ceases. Where the obstruction is incomplete the urine accumulates, and in course of time distends the kidney, causing *hydronephrosis*. Where it is complete, the kidney atrophies. If there is only one kidney, a condition which was present ten times in 3,108 *post mortem* examinations, and must be relatively much more common in persons who have already suffered from calculus, total *anuria* occurs. The same result may follow from the simultaneous blocking of both ureters, a remarkable coincidence which has been several times recorded (HAEHNER, REICH). Absolute suppression does not always take place even in fatal cases of anuria, the irritated bladder ejecting from time to time a drachm or two of pale water-like or bloody fluid, containing very little of the normal urinary constituents. The general symptoms of *anuria* are distress, sleeplessness, vomiting and muscular twitchings, terminated by coma and death. The coma may be marked by the occurrence of deep sighing respiration, and by other phenomena resembling *coma diabeticum* (see Case 1, page 62).

The *diagnosis* of stone in the kidney is very difficult in many cases, and in these days of energetic surgery it has often happened that the kidney has been opened, or even excised, without any stone being found. *Pain* may be the only symptom present, as in a case recorded by Mr. Butlin where a calculus had existed for eight years without blood or pus appearing in the urine. Surgeon-Major G. H. Young has recorded a case of malarial nephralgia, presenting attacks of renal colic with retraction of the testicle, but normal urine, which was eventually cured completely by quinine. Dr. Nestor Tirard has reported a case in which the pain, which resembled that of calculus, appeared to be caused by firm cicatricial adhesions between the colon and the kidney. When in addition *blood* or *pus*, or both, are present in the urine, the diagnosis may appear more certain, but Dr. Ralfe has furnished an example where these were associated with paroxysmal pain in the right kidney and retraction of the kidney, but the patient was cured of all his troubles by opening an abscess which lay between the rectum and the bladder, and communicated with the bladder cavity. *Hæmaturia* alone may be the only indication of a calculus, but even when its renal origin can be determined beyond doubt, as in these days is possible by means of the cystoscope, it may be due to malignant

disease of the kidney, epithelioma in the renal pelvis, or as in a remarkable case recorded by Senator, which he calls renal hæmophilia, the kidney after excision may appear perfectly healthy. Even when associated with pain hæmaturia does not necessarily point to the presence of a stone, as a slightly displaced kidney may give rise to these symptoms. The difficulty of diagnosis is very great. I had under my care for some years a young woman, whose attacks of pain and hæmaturia came on first after being struck in the loin by the angle of a wall. The pain and hæmorrhage ceased after rest in bed, and for some years she seemed to get relief from the use of a pad and bandage, but at last her troubles returned in such an aggravated form that I recommended nephrorrhaphy, or stitching the kidney to the loin. She went under surgical treatment for this purpose, but when the kidney was exposed it was explored, and an oxalate of lime calculus as large as a blackbird's egg found and removed!

Pus in the urine, when undoubtedly of renal origin, points to pyelitis, and although pain in the loin and irritability of the bladder may be present, yet on opening the kidney no stone may be found! We require therefore, in addition to pain and the presence of blood or pus in the urine, a history of the *previous passage of a calculus* to make the diagnosis of stone in the kidney a pretty safe one. In the absence of such a history our diagnosis must rest upon a very careful examination of the patient, and upon the exclusion of other possible causes for the symptoms. An exploratory operation is often justified by the result and may be undertaken:—

(1,) Where a perinephric abscess has formed.

(2,) Where there is a renal tumour, with fever, and pus or blood in the urine.

(3,) Where pain is so persistent or so frequently renewed, in spite of medical treatment, that the patient's health and comfort are seriously impaired.

(4,) Where there is persistent hæmorrhage from the kidney.

(5,) When suppression of urine has occurred.

A man was admitted into hospital some years ago, supposed to be suffering from spinal caries. There were several sinuses which led down to a rough body, believed to be a sequestrum; it was removed and proved to be a renal calculus. The man made a perfect recovery.

Plicque relates the case of a woman who suffered from severe pain in the left side of the abdomen, radiating into the

hip, vulva and rectum, while a painful oval tumour as large as a nut could be felt by vaginal examination in the left parametrium. Left salpingitis was diagnosed and treated by morphine injections and poultices; next morning she passed two small stones in the urine, and only a little tenderness remained at the site of the tumour!

The *prognosis* of stone in the kidney is not as a rule unfavourable, but it is grave when:—

(1,) The urine is suppressed.

(2,) The functions of both kidneys are seriously impaired, as indicated by great diminution of the urea excretion.

(3,) When a large perinephric abscess has not been recognised until septic fever has produced serious wasting and loss of strength.

Suppression of urine though grave is not always fatal, and recovery is possible even after it has lasted many days. My late colleague, Dr. Russell, recorded a case in which the suppression passed away after twenty days' duration, and the patient lived for more than two years.

Renal failure, if correctly determined, must prove fatal before long, and the importance of ascertaining definitely the daily excretion of urea cannot be too strongly stated.

In the third case there is room for hope, but the sooner the operation is performed the better, and the risk of failure must not be overlooked. When undertaken early the opening of a perinephric abscess is as favourable as any similar surgical procedure can be, and it is to be hoped that these unhappy cases, recognised too late, may in future be seldom seen.

Very rarely the presence of a stone in the pelvis of the kidney appears to be the starting point of malignant disease, such cases having been reported by Norman Moore and others. It has been suggested that tuberculosis of the kidney is also favoured in the same way, and although it is not common, it may possibly be true at times; more commonly tuberculosis of the kidney originates independently of calculus.

The *treatment* of stone in the kidney must be considered under (1,) prophylaxis; (2,) medical and (3,) surgical means for removing the stone; and (4,) management of renal colic.

Prophylaxis.—From what has been said of the causes of stone, it may be judged that we do not possess the groundwork for a scientific prophylaxis.

The most common forms of stone, uric acid and oxalate of lime, are associated with the uric acid diathesis, and it is

certain that the precipitation of uric acid depends upon diminished alkalinity of the blood. Such persons should be dieted by being warned to eat very sparingly of butchers' meat, and to eschew sugar, vinegar, sweet wines and malt liquors; they should live mainly on vegetables, fruits, farinaceous food, game, poultry and fish, drinking light dry Moselle, or Bordeaux wine, or good whisky well diluted with aërated alkaline water. If the water of the district is hard, they should drink aërated distilled water to which potash or soda may be usefully added, and distilled water or boiled and filtered rain water should be used for making tea, coffee, etc. Exercise and cold baths, or the Turkish bath must not be omitted.

Steady adherence to an absolute milk diet has often cured an inveterate tendency to stone, but most patients require to suffer much before they accept such a regimen for the remainder of their lives. Yet there have been sufferers who were glad to find relief even on this fare.

The prophylactic treatment of cystin calculus should be by the regular administration of sulphate of magnesia or sulphate of soda as an aperient, together with salol (gr. x), or β-naphthol (gr. v) in cachets two or three times a week.

The *medical* treatment of stone in the kidney is of two kinds: (1,) solvent; (2,) expulsive. The *solvents* in common use are alkalies, or alkaline mineral waters. It is best to give a full dose of alkali at bed time: for example, forty grains of citrate of potash, or ten grains of citrate of lithia in half a tumbler full of potash water at bed time. I do not think the alkaline mineral waters effect very much by themselves, but they may help. The persistent use of distilled water, originally recommended by Murray, has answered very well in certain cases, but it is absolutely necessary that it be the sole vehicle employed for all beverages including tea and coffee. It may be obtained as potash, soda, or other mineral waters, and may be mixed with whisky or light wine.

An extended trial of piperazine and lysidine, reputedly powerful solvents of uric acid, has left me doubtful of their value.

The action of solvents is probably little marked except on uric acid stones, although Christison used to point out that the insolubility of the crystalline basis of a calculus was not proof of its impregnability to the attacks of drugs, as the

integrity of the calculus depends upon its organic cement which may be loosened by chemical means.

The *expulsives* in use are turpentine, belladonna, and oil of sandal wood. Ralfe gave turpentine in ten minim doses in capsule; Murray recommends twenty minims of tincture of belladonna every hour until the calculus is expelled or physiological symptoms of belladonna poisoning result; Philbert uses four ordinary capsules of oil of sandal wood for a dose. These remedies, if effectual, bring on an attack of renal colic, so that the patient must be warned of their possible effect, and he must be a bold man who does not hesitate to persevere in this line of treatment.

The surgical measures to which we have recourse are: (1,) manipulation; (2,) incision.

Manipulation was successfully performed by Mr. W. H. Bennett, who managed to feel a stone in the kidney and manœuvre it down the ureter into the bladder; but this great achievement has not been repeated to my knowledge.

Incision, or nephrolithotomy, must be the only means of removing large stones, and in all cases when the kidney has been exposed it should be opened and explored, as a stone may otherwise easily escape detection; in fact this has happened even after opening.

Renal colic being one of the most painful maladies from which human beings suffer, anodynes must stand first in our list of remedies. The first thing to do is to give ⅓ grain of morphine hypodermically, except where there is good reason to believe the kidneys are badly diseased, and then we must rely on hot fomentations or the application of dry heat, or chloroform inhalation. Large doses of belladonna may be tried for the purpose of relaxing the ureter. The patient should remain in bed until all the pain has disappeared.

Impaction of the stone in the ureter, with or without suppression of the urine, can only be treated by surgical means. The lateral abdominal operation advocated by Mr. Knowsley Thornton is to be preferred, as it gives better access to the whole length of the ureter.

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CHAPTER XXIV.

HYDRONEPHROSIS, PYONEPHROSIS, PYELITIS.

THE name *hydronephrosis* was originally invented by Rayer, to denote those cases of cystic kidney, in which the cysts are large, the contents water-like, and the apparent cause some obstruction to the outflow of urine. The enlargement affects first the pelvis, afterwards the calyces, and expands these at the expense of the kidney substance, which is stretched over them and converted by interstitial inflammation into fibrous tissue.

Out of 3108 *post mortem* examinations, I met with 38 cases of hydronephrosis, or in 1·2 per cent. In 19 of these the affection was bilateral, and of the remainder in 12, or 63 per cent., the left kidney only was involved. In more than half, the cause was obstruction to the urethra from stricture, or enlarged prostate or phimosis. Next, most commonly it was due to the pressure of some growth, *e.g.*, cancer, aneurysm or hydatids, upon the ureter, or to occlusion of the ureter by the traction of *procidentia uteri*. Much more rarely it was due to calculus in the bladder, although in one instance double hydronephrosis originated in this way; or it was the consequence of an injury, displacement of the kidney, congenital malformation or malposition of the ureters.

Both ureters have been found bent twice upon themselves, while on the right side a constriction existed at the second curve (LIVINGSTONE); or the ureter opens into the pelvis of the kidney above its lower extremity, or at too acute an angle, or is guarded by valves (HARRINGTON SAINSBURY), or the ureter may be compressed by a branch of the renal artery crossing it.

Mobility of the kidney may give rise to hydronephrosis by kinking the ureter, and it is especially in these cases that we get the symptoms of intermittent hydronephrosis to be described further on.

Among the rarer causes is that described by Knowsley Thornton, where the ureter was obstructed by a papillomatous

growth the size of a pea, capped by an olive-shaped dark-brown calculus.

The renal opening of the ureter has been found to be only a mere pin-point. Obstructions in the urethra and bladder would, presumably, cause double hydronephrosis, but there are curious exceptions to this rule. A boy with congenital stricture of the urethra was found to have hydronephrosis of one kidney, and granular contraction of the other (HUMPHREYS).

It may be thought that stricture of the urethra being a somewhat remote, although common cause, is not capable of causing more than moderate expansion of the kidney. Undoubtedly it is not associated with the largest tumours, but it may convert the kidney into a multilocular cyst with an outer wall not more than a quarter-of-an-inch thick.

A rare cause of hydronephrosis is *diabetes insipidus* (see p. 384), where the condition is undoubtedly induced by the quantity of urine secreted exceeding the rate of outflow and so causing retention, which in course of time gradually expands and destroys the kidney.

Mobility of the kidney is not a common appearance in the *post mortem* room, perhaps because the renal fat when cold holds the kidney more firmly than it did during life. It is perfectly certain that some cases of hydronephrosis have presented no visible obstruction to the outflow of urine. Küster suggests that these cases may have been originally due to catarrh of the pelvis of the kidney. He says that it is not conceivable to have such a catarrh without some swelling of the mucous membrane by which the opening of the ureter becomes narrowed. During abundant secretion of urine, especially after drinking large quantities of fluid, a disproportion must ensue between the amount secreted and that leaving the kidney, and retention follows. When the intra-renal pressure is increased the swollen mucous membrane which is movable on the submucous layer, slips down in the direction of the stream, just as the mucous membrane of the bowel does in a hernia, and a fold is formed which constitutes a growing obstruction to the outflow of urine. When the distension reaches a certain degree, it produces a change in the position of the kidney (SIMON), and causes complete occlusion of the ureter. Whether the secretion is more or less purulent depends upon the degree of suppuration which previously existed.

The anatomical causes of hydronephrosis having been suffi-

ciently described, it only remains to discuss the resulting changes in the kidney itself. The distension of the organ varies in degree, in its minor forms amounting to more or less dilatation of the pelvis and calyces with flattening of the renal papillæ; but in the more pronounced cases the dilatation of these cavities increases until the kidney forms a lobulated sac, varying in size from a small cocoa-nut to a cyst filling half the abdominal cavity. On section the cyst is multilocular from the persistence of the walls of the calyces. It is lined throughout with a smooth mucous membrane, and there may be no trace of renal tissue recognisable by the naked eye. The change in the true kidney substance is due to interstitial inflammation, which destroys the tubules and glomeruli, replacing them by indifferent connective tissue.

Hydronephrosis, as already stated, is very often bilateral, but one kidney may be more advanced than the other, or one may be hydronephrotic and the other granular and contracted. It has happened more than once that one half of a horse-shoe kidney has become the subject of hydronephrosis, while the other remains healthy.

From what has been said it is plain that the obstruction in hydronephrosis is never complete or permanent, at least in the earlier stages, and where complete closure or obliteration of the ureters is found, *post mortem*, this must have supervened after the development of the sac.

Hydronephrosis occurs so frequently as a complication, or result of other more obvious conditions, that it is not uncommon for it to pass unsuspected or at least undiagnosed during life. Its earlier stages give rise to no symptoms, but later on there may be some pain or tenderness in one or both hypochondria, with vomiting, and perhaps shivering. In some cases severe vomiting, diarrhœa and abdominal pain, have been such as to recall the gastric crises of locomotor ataxy. The urine is rarely normal; it usually contains a little albumen and a few pus cells, while in the more advanced cases the amount of urea becomes greatly reduced. Uræmic coma is the usual termination.

The cases that are distinctly recognised during life are those in which hypochondriac pain leads to the discovery of a renal tumour. When large and distinctly fluctuating the diagnosis is easy, but in small cysts this sign may be absent, and the nature of the tumour can only be determined by aspirating some of its contents and testing for urea, although in old sacs this

may have disappeared. As a rule renal tumours have the colon in front of them, and do not move on respiration; but on the right side the colon may not have this relation to any appreciable extent, and movement on respiration may take the colon. The chief difficulty is to differentiate such a place (FÜRBRINGER, KÜSTER, ISRAEL). Hydronephrosis in a movable kidney is also an exception to this relation to tumour from an ovarian cyst, but on vaginal examination no drawing-up of the uterus is found.

The sac may discharge spontaneously through the ureter and never refill, or it may rupture into the peritonæum, or even through the diaphragm into the lung, or it may suppurate and become *pyonephrosis*.

Much attention has been lately directed to *intermittent hydronephrosis*, where the contents of the sac are discharged through the ureter from time to time, the tumour disappearing temporarily, but returning again. The usual history of these cases is that the patient goes about with a gradually increasing dragging pain in one side of the abdomen until forced at length to go to bed; after a few days' rest the symptoms disappear and the patient gets up again.

When under observation it is noticed that as the pain increases the urine diminishes, and a tumour forms in one or other hypochondrium. After going to bed, the urine becomes greatly increased and the tumour disappears. These cases were first explained by Landau, and by him attributed to mobility of the kidney, and kinking or twisting of the ureter. From the description given by Küster of the mode in which hydronephrosis is brought about, when no anatomical obstruction exists, it may be understood that position plays an important part in the process, and it is easy to realise the sequence of events which gives rise to this form.

CASE 81.—Jane ———, 47, was admitted on July 21st, 1888, complaining of a tumour in the right side of the abdomen. Eleven years before, about a week after a confinement, she had noticed a tumour, the size of a hen's egg, just under the costal arch. There is no doubt that this was a floating kidney; it was present for a day only and did not return for about three months, but she noticed it after this three or four times a year. It was a little painful but was not tender. Two years ago she observed a tumour in the right iliac region which gradually increased in size, rising higher up in the abdomen, and gradually disappeared after about three weeks. Six weeks later it returned, and continued to come and go in the same way at intervals of three, four, or five weeks. Then for a time the intervals became longer, but in April 1888 she grew worse, and went into the Workhouse

Infirmary, when she was told she had a "phantom tumour." On admission under my care, an oval smooth tumour could be felt in the right hypochondrium. It did not fluctuate, was painful and tender, and it did not move on respiration. The urine was very scanty, only 2½ oz. being passed in sixteen hours after admission, and this contained a little albumen with leucocytes and squamous epithelium. The following day she had passed 52 oz. of urine and the tumour was much smaller. After a few days she was allowed to get up and the tumour returned, she was then sent back to bed and it disappeared. I was absent from home at the time of her admission and when I saw her there was no tumour to be felt, and as she felt quite well she was discharged. On September 29th, she was readmitted with pain, vomiting, and a large rounded swelling in the right side of middle line of the abdomen. The swelling was movable and could be manipulated into the right hypochondrium when she was under an anæsthetic. It was aspirated, and bloody fluid drawn off which contained after removing the blood and albumen, 0·7 per cent. of urea, and gave crystals of nitrate of urea. The next day she had passed 27 oz. of bloody urine and the tumour was gone! It did not return, and the patient was discharged, after the nature of her ailment had been explained to her; but she was advised to go to bed whenever it troubled her. In addition she was provided with a well-fitting belt and pad, by which she kept fairly comfortable, and in June 1889, she was seen to be going on very well, having had only one relapse.

This condition is much more common in women than men, in the proportion of 4 to 1, and occurs more often on the right side than the left, in the ratio of 3 to 2, this being apparently dependent upon the greater frequency of mobility of the right kidney in women. The pregnant uterus may so compress the ureter as to prevent the recurrence of these attacks, or it may make them more frequent and more painful. On the other hand the presence of hydronephrosis places the pregnant woman in danger of abortion or premature confinement, of uræmic convulsions, or of death from suppression of urine.

Intermittent hydronephrosis may become permanent in consequence of fibrous adhesions forming around the sac and strangling the ureter. Infection of the sac may take place at any time while the ureter remains open, converting the condition into *pyonephrosis*, accompanied by more or less septic fever. Some cases of parovarian cyst may present these phenomena of temporary disappearance followed by increased secretion of urine owing to rupture of the cyst wall and discharge of its watery contents into the abdominal cavity, but the differential diagnosis is not difficult.

The treatment of hydronephrosis may be (1,) *palliative*, or (2,) *radical*. Palliative treatment is only available in intermittent cases, where a pad and bandage may keep the kidney in place and prevent recurrence, or in very old standing cases

where the health of the patient, or the great probability of adhesions, may make extirpation out of the question, and a belt the only resource.

Radical cure may be effected in the early stages of intermittent hydronephrosis by stitching the kidney in its place. Where mobility is not in question the kidney may be (1,) opened and drained, or (2,) extirpated. Although the former operation has effected a cure, as in a case reported by Tuckwell and Symonds, as a rule a urinary fistula remains and extirpation is to be preferred, but before this operation is sanctioned, we must be sure that the patient has a sufficiently sound kidney on the other side. We should be guided in our decision by the absence of pain, tenderness, or tumour on the presumably sound side, and above all by the elimination of a sufficient quantity of urea. Where pyonephrosis exists, extirpation is all the more urgently indicated, but it is too often impossible from the presence of adhesions; it may be desirable to make an incision to let out pus, but such an operation is rarely attended with any satisfactory results.

Rupture of the sac into the peritonæum must be treated by prompt abdominal section, an operation which may save the patient's life, as was accomplished by my friend Mr. J. W. Taylor, of Birmingham.

PYELITIS is suppurative inflammation of the pelvis of the kidney. It was present in 35 instances out of 3108 *post mortem* examinations, and of this number it affected both kidneys in 28, or 80 per cent. Where one kidney only was affected, this was commonly the left—L. 5; R. 2.

Its most common cause is cystitis, which accounts for fully half the cases. Next in frequency, but only accounting for about one sixth, is stone in the kidney. The other causes are tubercle, acute infective processes, such as enteric fever, pneumonia, scarlatina, diphtheria, pyæmia, small-pox, infection in association with pressure upon the ureters, cancer of the bladder, etc. The *pathogenesis* of the condition is not always the same; where it occurs in connection with diseases of the urinary passages, it is no doubt set up by infection through the ureters, but in the infectious processes the microbes reach the kidney through the blood.

The most common symptom of pyelitis is pain in the loin, which may extend to both sides, and radiate down the leg. Pus is found in the urine. There may be shivering, yawning, vomiting, and frequency of micturition; in fact, the last

symptom may be the most serious trouble, and may be present when there is no cystitis, but giving rise to all the phenomena of irritable bladder. If the pyelitis is uncomplicated by calculus or cystitis, the urine is acid and contains no crystals. Its differential diagnosis from calculus has already been considered. The condition may remain stationary, or go on to pyelonephrosis, or to perinephric abscess, or may subside and become cured, but its course depends very much upon the cause. The cases which are most favourable are those which have originated in connection with infective processes, and are not complicated by any disorder of the lower urinary tract.

The *treatment* of these cases is by rest in bed, milk diet, and the internal administration of alkalies and sandal-wood oil. Rest has a remarkable effect in alleviating the pain. Where other conditions exist which have excited the inflammation, these must receive appropriate treatment, which is mainly surgical, but simple cystitis improves greatly under this treatment.

I generally order :—

℞ Liq. Potassæ - - - - ℥ij
Ol. Santal. flav. - - - ℥ij
Aq. Cinnamomi ad. - - - ℥viij
M.

Sig.—Two tablespoonfuls three times a day.

Surgical treatment by drainage is absolutely useless, and incurs great risk of a urinary fistula. In mild cases, which we call pyelitis, a more serious operation is not justifiable, but in pyelonephrosis extirpation is the only means of cure, and if it is to be successful, must not be delayed long. Where the pyelitis causes constitutional symptoms which cannot be controlled by rest, surgical interference is both proper and necessary.

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CHAPTER XXV.

HÆMATURIA, HÆMOGLOBINURIA.

THE presence of *blood* in the urine is a symptom common to a number of pathological conditions, differing essentially in their seat, nature and relationships. It may appear in a corpuscular or non-corpuscular form; the former is called *hæmaturia*, the latter, *hæmoglobinuria*.

Blood may be mixed with the urine as it leaves the body, for example during menstruation, or whenever there is vaginal or uterine hæmorrhage, or sometimes by bleeding from the rectum due to piles, etc.

Hæmorrhage from the urethra may be caused by villous growths or depend upon local congestion or injury. The blood is bright coloured, it may appear independently of micturition or at the beginning or end of the act, and is often accompanied by local pain and other symptoms pointing to its source.

Hæmorrhage takes place from the bladder when this is the seat of inflammation, ulcer, villous growth, cancer, stone, prostatic congestion, parasites, etc. These conditions have their own special symptoms, but the diagnosis of diseases of the bladder has acquired greater precision since the introduction of the cystoscope.

Hæmorrhage from the kidneys is due to numerous causes:—

(1,) *Local lesions*: External injury, twisted or movable kidney, calculus, tubercle, cancer, syphilis, embolism, parasites, congestion, inflammation (Bright's disease).

(2,) *Symptomatic*: Blood diseases (purpura, scurvy, leucocythæmia, hæmophilia), specific fevers.

(3,) *Toxic*: Turpentine, cantharides, garden rhubarb (Boyd).

(4,) *Neurotic or vicarious*: Hysteria, insanity, asthma, menstruation, hæmorrhoids.

Blood from the renal substance is generally moderate in amount, altered in colour, and under the microscope is seen in the shape of casts of the renal tubules. Blood from the pelvis of the kidney may be more profuse, and form casts of the ureter, but never casts from the tubules. When blood has

been mixed with urine for some time its bright red colour becomes changed to dirty brown, and the urine may present all gradations of tint from a deep porter colour to mere smokiness. This change is due to conversion of the blood colouring matter from oxyhæmoglobin to methæmoglobin. Unaltered blood in the urine, even when present in small amount, may be recognised by its characteristic dichroism, that is, by reflected light it appears red, while by transmitted light it is green. The various tests by which the presence of blood in the urine may be detected are described in the chapter on the Clinical Examination of the Urine.

External Injury causes laceration of the kidney substance, which if extensive may call for extirpation of the organ; in most cases the wound heals and recovery takes place. The diagnosis presents few difficulties, and the treatment must depend upon the amount of hæmorrhage, which, if great, will cause a tumour in the flank from effusion into the neighbouring tissues. The treatment must be rest, an ice bag to the part, ergotin subcutaneously, and in the last resort extirpation.

CASE 82. *Hæmaturia after Injury.*—William C., aged 35, stone-mason, was admitted into the General Hospital on December 10th, 1886, complaining of pain on the right side under the short ribs. A week ago he was crushed between a stone and some scaffolding just in the seat of pain; and the next day there was pain on passing his water, which was "muddy" looking. His personal and family history were good; he was well built and muscular, his heart sounds were feeble, his teeth were defective, his tongue dry and furred, and he complained of want of appetite with a foul taste in his mouth. When he first came to the hospital on December 10th, he brought a specimen of urine which was red with blood, and in which there was a clot rather flattened in shape, about three-quarters of an inch in length, and three-sixteenths of an inch in diameter, probably a cast of the ureter. On microscopical examination the fluid contained "masses of granular matter, probably fibrinous, enclosing leucocytes and indistinct red blood corpuscles." Urine examined four hours and a half after it was passed contained numerous red cells, while the fibrinous masses were few and small. With rest in bed and a pad and bandage, the blood gradually disappeared, there being none on his discharge on January 1st.

Movable Kidney.—Closely connected with the foregoing are cases of persistent or intermittent hæmaturia dating from a blow or fall. It is supposed that the organ is partially displaced and rotated on its horizontal axis, so as to twist the vessels at the hilus, thus compressing the vein and causing passive congestion. The following case shows how severe, as well as persistent, such cases may be.

CASE 83. *Hæmaturia from Displaced Kidney, following a Fall.*—A. R. B., aged 23, clerk, was admitted into hospital on November 2nd, 1886, complaining of hæmaturia and pain in the loins, chiefly on the left side, aggravated by exertion. Four years before he had a bad fall from a bicycle, which was followed by hæmaturia. This passed off, to return in March, 1886, after working at a forge in a metallurgical class at the Midland Institute. Finally, a few weeks later he was nearly run over, and in springing out of the way he seemed to strain his back. Since that time the hæmaturia persisted, in spite of rest in bed for fourteen weeks on milk diet. The quantity of urine was at no time diminished, and there was never any dropsy. His previous health had been good. On admission there were no physical signs of disease or high arterial tension. The ophthalmoscopic appearances were normal. The urine was always sufficient in quantity, and contained a normal amount of urea. Blood casts were constant, but hyaline casts were rare, and an epithelial cast was only seen once. Mr. Langley Browne, of West Bromwich, under whose care he was, examined his bladder with negative results. The hæmaturia persisted, but for three weeks during the summer there was an intermission. His general state was fairly satisfactory, but he was depressed and anæmic. He was treated unsuccessfully for a long time by a pad and bandage, and all kinds of hæmostatic drugs, but ultimately got quite well.

The next case has no history of injury, but probably belongs to this class, as the hæmaturia was relieved by rest and cured by a pad and bandage.

CASE 84. *Hæmaturia due to Renal Displacement: Temporary.*—B. B., aged 18, warehouse boy, complained of pain in left lumbar region, which had existed for five or six years. He characterised the pain as dull and aching, worse when walking than while sitting. His previous health had been quite good, but his bowels were very confined. His urine was pale, clear, and contained a trace of albumen but no blood. With rest and attention to his bowels the pain left him, but on returning to his duties the pain returned, and the urine contained blood. He was then ordered to wear a pad and bandage, and a fortnight later was quite free from pain and the urine free from blood. Six weeks later this improvement was maintained, though there was still a trace of albumen. The diagnosis in this case depends mainly on the results of treatment, as there was no history of a blow or fall; but it is supported by the disappearance of the hæmorrhage during rest.

The employment of an efficient bandage is of the utmost importance for the successful treatment of these cases.

Calculus.—A medical friend of gouty habit and a great sufferer from oxaluria was getting into his brougham one day, when his horse started and flung him on the back seat in such a way as to bring on an acute pain in the left loin as if he had strained a muscle. Later in the day he vomited, and the pain was so great at night that he took opium to relieve it. The urine became bloody. In the course of twenty-four hours he passed a small oxalate of lime calculus, and his troubles ceased. This case shows that hæmaturia after a strain or blow may be caused

by the displacement of a calculus which had formerly occupied some position in which it gave rise to no symptoms. Had the stone not passed the cause of the hæmorrhage would have remained obscure or it might have been put down to partial displacement of the kidney. The symptoms of renal colic are tolerably characteristic. The pain shooting down towards the groin, with vomiting, and retraction of the testicle, are not met with in any other condition. It is noteworthy that the pain in biliary colic does not pass downwards to the abdomen, but radiates round the thorax, and is especially localised at a spot below the right shoulder blade. A medical friend whom I recently attended for biliary colic tells me that the worst pain of all was a feeling as if three or four vertebræ were being gripped by a pair of pincers. Confusion between these two conditions is impossible if hæmaturia is looked for and relied upon, as I believe it may be, as a constant symptom of renal colic, but it may not always be present in quantity sufficient to reveal itself to inspection with the naked eye. Conversely I hold that the diagnosis of calculus in the kidney is incomplete until hæmaturia has occurred.

The following case, probably also an example of renal twist or displacement, illustrates the difficulty of diagnosis of calculus from the symptoms of pain and hæmaturia alone.

CASE 85. *Hæmaturia due to Renal Twist.*—Mrs. M., aged 43, was sent to me by Dr. Lycett, of Wolverhampton, with the history that she had been ill for four or five years, and had been told by her previous medical attendant and a physician in Birmingham that she had Bright's disease. Her symptoms were pain at the bottom of the back, worse on the left side, shooting down towards the groin, with albumen in the urine. She was a very stout woman, who had had six children very rapidly. At the time of her marriage she was very thin, but got stout during each pregnancy, becoming thin again after the first and second confinements She was never strong. There had never been any dropsy. The urine had been dark at times, but never like porter. Dr. Lycett had found that the urine was normal in amount and specific gravity, that the urea excretion was not diminished, that there were never any renal casts, that the albumen was very small in amount and was frequently accompanied by blood; oxalates and uric acid crystals were very abundant. As she made extreme complaints of the pain incapacitating her from all her duties, an exploratory incision was made by Mr. Tait, but no calculus could be found. The wound healed perfectly, and she left Mr. Tait's hospital quite free from pain and hæmaturia, but these came on again in a few weeks. I recommended an abdominal belt and pad, and this she wears, but still complains of pain. Her abdomen is very large, and the walls are very relaxed, so that it is difficult to apply pressure efficiently to the kidney. She is, however, no doubt much better than she was, and is certainly not the subject of Bright's disease.

It may be contended that the negative results of operation do not absolutely exclude calculus. In a case treated at one of our hospitals I believe a stone was passed *per vias naturales* after an exploratory incision had been made without success, so that we must allow that even surgeons are fallible, and we know that a stone of small size may give rise to marked symptoms without getting into the infundibulum.

Tubercle.—Hæmaturia in tubercle is accompanied by pus and shreds of renal tissue. Tubercle most commonly causes pyelitis, and there is much more pus than blood in the urine. The diagnosis of tubercle depends largely on the constitutional condition and on family history.

Cancer.—Hæmaturia is not always present in cancer; when it is, it is very profuse. The diagnosis in some cases is easy, as a tumour may be felt, and deposits in other organs can be made out. Microscopic examination may show "cancer" cells, but these cannot be relied upon. In some cases the differential diagnosis from calculus is very difficult. The hæmorrhage is, perhaps, more profuse and persistent. The subjects of cancer may last a long time in fair health; one patient of mine had suffered from hæmaturia for four years before I saw him, and lived quite two years afterwards. Mr. Chavasse made an exploratory incision under the belief (which I shared) that he had a calculus He recovered from this and died some time afterwards, the *post mortem* examination, at which I was not present, showing cancer of the kidney and liver.

Syphilis.—Gummatous deposits in the kidney are well known in the *post mortem* room, but their clinical phenomena have not been fully made out. In this respect the following case of syphilitic ulceration of throat accompanied by hæmaturia is of interest.

CASE 86. *Syphilitic Sore Throat: Hæmaturia.*—A. H., aged 19, an inmate of the Edgbaston Asylum for the Blind, was admitted into hospital on March 10th, 1887, complaining of her water being high-coloured and scanty and of deafness. Three years ago she suffered in the same way. She had been blind from her birth, and since nine years of age had been an inmate of schools for the blind. Her mother was dead, but she could not tell the cause of her death. Her father and the rest of the family were living and healthy. She was a well-nourished girl, rather delicate looking. Cheeks flushed; both corneæ disorganised and staphylomatous; no œdema anywhere; thoracic and abdominal physical signs normal; temperature 98·6°; pulse 96; respiration 24. Urine the day after admission 32 ounces, specific gravity 1022, acid, turbid reddish in colour; deposit consisted of red and white blood-corpuscles, urates, and squamous epithelium. On boiling there was a thick cloud of albumen, and the chemical

reactions for blood were present. A very few hyaline casts were seen on only one occasion. The hæmaturia persisted for several weeks, but nine days after admission she began to complain of her throat, and liquids tended to come back through her nose. The pharynx and tonsils were very congested and covered with sticky muco-pus. Two days later a sloughy eroding ulcer appeared in the soft palate to the left of the uvula, which I have no doubt was syphilitic. In answer to inquiries she stated that her throat had been sore ever since the previous August. The ulcer was treated by the application of acid nitrate of mercury, and the patient took a mixture containing the perchloride of mercury, combined with the perchloride of iron. The throat got slowly better, and on April 18th was nearly well, while at the same time the blood is noted to be "much less." On April 30th the hæmaturia had entirely disappeared, and she was discharged cured.

Embolism.—Embolism of the kidney is not an uncommon accident in heart disease, especially in vegetative endocarditis, also in pyæmia. Hæmaturia occurring under these conditions may safely be attributed to embolism.

Parasites.—Hydatid cysts in the kidney cause hæmaturia, and can only be recognised by the passage of fragments of hydatid membrane in the urine. Bilharzia hæmatobia, which generally attacks the bladder, may occur in the pelvis or substance of the kidney, and manifests itself by the characteristic ova and embryos in the urine.

Congestion.—Congestion may be active or passive. Active congestion is often only the initial stage of acute inflammation, a condition which very rarely attacks healthy kidneys, except during the course of acute specific diseases; for example, scarlatina, diphtheria, tonsillitis, typhoid fever, etc. But such congestion also occurs when the functions of the skin are seriously interfered with, as by extensive burns, or more commonly by chilling of the surface as in bathing, exposure to cold, etc.

A few years ago a young man consulted me, saying that he believed he was passing blood. He had been to a swimming bath, and after returning home, noticed his urine was bloody. This was on Saturday, and on Monday, when I saw him, the urine contained only a trace of blood. By Wednesday the urine was normal. This patient told me that his brother had consulted Dr. A. H. Carter for hæmaturia following exposure to wet after playing football.

The following case of persistent hæmaturia appears to me due to a special susceptibility to chill. These cases show that corpuscular blood may be passed as the result of chill.

CASE 87. *Hæmaturia due to Chill.*—S. A., aged 19, came to me in December, 1886, complaining that his urine had been bloody for the last three weeks. Eighteen months before, in June or July, he first passed coffee-coloured urine for one day after playing cricket. He could not remember any blow or fall having preceded it. He had no shivering fit, and felt quite well. His previous health had been good, but he had been very subject to chilblains on his feet in summer as well as in winter, and his hands and feet easily get cold. He was a well-developed, fairly well nourished lad, with no objective signs of organic disease, but his face and hands had a congested and cyanotic look. He suffered no pain or uneasiness, had never had syphilis, jaundice, or dropsy, and had never been out of this country, but he had been at Cambridge for the last two years. The urine was dark amber, acid, 1018, with brown, flocculent deposit, composed of red and white blood corpuscles, spermatozoa, blood casts, a few hyaline casts, and granular matter. The quantity of urine was 50 ounces, and the excretion of urea 300 grains *per diem*. The quantity of albumen was not more than was accounted for by the blood. In spite of careful clothing and staying indoors, the hæmaturia persisted. At the beginning of the May term he went back to Cambridge, and kept much the same, well in himself, but the urine persistently bloody, though never very bad. It was no better in the very hot weather than it has been since it has turned colder. He has been playing tennis, and taking other exercise freely. I saw him again on October 8th, and found no change except an occasional intermission in the pulse, which was rather small. The urine was amber, acid, 1014, contained blood, and one-twelfth column of albumen. The deposit consisted of blood, oxalates, a few blood casts, and hyaline casts with blood corpuscles sticking to them. He has since entirely lost his liability to these attacks, and he now looks a strong man.

Passive Congestion.—Venous engorgement, consequent upon liver, heart, or lung disease, may cause slight hæmaturia. The condition is easily understood, and readily recognised.

Bright's Disease.—In acute nephritis, more or less hæmorrhage occurs, and persists throughout the acute stage. The diagnosis depends upon the other evidences of Bright's disease—for example, dropsy, and the presence of epithelial casts in the urine. In chronic Bright's disease, hæmorrhage is not constant, but may occur at any time. The amount is usually moderate, but, in rare instances, may be alarmingly profuse and fatal. The recognition of the nature of the case depends on the presence of casts in the urine and other confirmatory signs—such as polyuria, low specific gravity of urine, cardiac hypertrophy, high arterial tension, albuminuric retinitis, etc.

Symptomatic Hæmaturia.—Hæmaturia occurring in connection with specific diseases, such as yellow fever, malarial fever, and cholera, or in the course of blood diseases, such as purpura, hæmophilia, scurvy, and leucocythæmia, depends for its correct diagnosis on the recognition of these diseases, each of which possesses well marked symptoms and definite clinical relations.

CASE 88. *Purpura Hæmorrhagica; Hæmaturia; Recovery.*

Harold N., ætat. 3, admitted into hospital May 27th, 1888, with purpuric rash and hæmaturia. He came of a healthy family with no evident tendency to rheumatism, hæmorrhage or bruising. A year ago he had measles but had been quite well since. He had never previously had any spots on his skin, nor had his mother noticed that he bruised easily, or had ever passed blood before in his urine; he had been well fed, mostly on bread, pudding and potatoes with green vegetables about twice a week, but not much meat. For some time he had had a little cough in the morning. Six days before admission he seemed ill and did not play as usual; this continued all the week, and on the day before admission his mother noticed when washing him that there were a few spots on his skin which she took for flea bites. In the afternoon he began to pass blood in his urine, which was quite red; at night there were no more spots, but on the morning of admission she noticed spots all over his body and limbs, and his urine was still bloody. There had been no nose-bleeding, but on two mornings there was a thin line of dried blood on his lips. The motions had not been black or mixed with blood.

Patient was a well-nourished, rosy-cheeked, well-cared-for child. The spots varied in size from half an inch in diameter down to pins' heads, and were circular in shape and of a purple colour; they were most numerous on the right side of the abdomen, but were present more or less over the entire surface. There were two marks like bruises on the back. A little patch of dried blood was on the upper lip. The tongue was pale, bowels open, motions free from blood; temp. 99°, pulse 112, r. 28. There were a few râles and rhonchi over the chest and a little cough. The urine passed soon after admission was bright red in colour, and looked like pure blood; it was acid, and under the microscope there were numerous blood corpuscles. The blood taken by puncture from the skin contained a normal number of hæmocytes, but the hæmoglobin was reduced to 40 per cent. At noon he was given a draught containing half an ounce of turpentine and half an ounce of castor oil; he vomited a little at 3 p.m., and his bowels were open at night; the motion was free from blood. The next day the hæmaturia was quite as great.

May 29th.—Hæmaturia persisting; still blood on lips in morning; a fresh crop of spots noted on the left side of the body. At 11.45 a.m. he had ergotin, gr. j. subcutaneously. Blood again examined, and found to contain 120 per cent. of red corpuscles; from one to three leucocytes in the field at once. In the evening, as the hæmaturia was unchecked, the injection of ergotin was repeated. At 9 p.m. he vomited and passed more bloody urine. His temperature ran up to 100·6, p. 144, r. 30, and he complained of thirst and cough. After midnight he slept well, and his temperature came down. The next morning (May 30th) the urine was only smoky. On the 27th Dr. Crooke examined the blood for micro-organisms, and attempted to make a gelatine cultivation, but the results were negative. There was no enlargement of the liver or spleen. The ergotin was repeated, as the urine continued to be smoky, till late in the evening, when it was free from blood. After this date (May 31st) there was no more hæmaturia, but a few fresh spots were noted on June 2nd, and on the same day there was slight epistaxis, the amount of blood lost not exceeding one drachm. The injections of ergotin were stopped on June 5th, and the same quantity, on pain, being given by the mouth for

two days longer. He was then ordered Parrish's syrup, and on the 11th was made an out-patient, but remained quite well and was discharged.

Toxic Hæmaturia.—Hæmaturia may follow the application of a fly blister or the internal administration of cantharides. The latter is seldom practised, but the drug has been recommended on quasi-homœopathic principles by Dr. Sydney Ringer for nephritis, and in that condition I have seen it even in one-minim doses cause distinct hæmaturia. When given for criminal purposes the dose is usually large, and the hæmaturia is accompanied by strangury, vomiting and symptoms of irritant poisoning. Turpentine does not generally cause hæmaturia, though the readiness with which the violet odour appears in the urine shows that it is absorbed and excreted by the kidney. I have had one very interesting example of hæmaturia due to this cause in a varnish maker who was sent to be examined for life insurance. He seemed a perfectly healthy man, but after he had gone I examined his urine, and found it contained a little albumen. I then noticed the odour of violets, and closer examination showed that the albumen was due to the presence of blood. There were no other evidences of renal disease, but there was certainly some special susceptibility to the action of turpentine, as this gentleman informed me that he was not personally engaged in the manufacturing processes, though he was much about the factory. I tried to follow up the case, but could not, as he abandoned the proposal.

The influence of garden rhubarb in causing hæmaturia was well attested by a quite voluminous correspondence in the *Lancet* a few years ago, many of the writers giving their own personal experience; the young forced vegetable seems to be free from this inconvenience. It is generally attributed to the production of an excessive quantity of oxalates, but this explanation has not been demonstrated.

Neurotic and Vicarious Hæmaturia.—I have no personal experience of these conditions. Laycock mentions hæmaturia as not uncommon in hysteria, but I have never recognised a case, though I have certainly met with one or two cases of hæmaturia in women which I have not ventured to class. Sir W. Roberts mentions menstruation, hæmorrhoids, and asthma as conditions in which vicarious or supplementary hæmaturia occurs, but I can only leave the matter without further comment, as I have never met with such cases. Dr. G. H. Savage states that hæmaturia may occur spontaneously in acute mania and general paralysis.

HÆMOGLOBINURIA.—This condition depends upon the dissolution of the red blood corpuscles in the body, and the presence of free hæmoglobin in the liquor sanguinis. Under these circumstances the hæmoglobin escapes through the Malpighian tufts, and appears in the urine. The determining causes of this change are not clearly known. Certain organic and inorganic poisons have this property of breaking up the blood corpuscles by direct action upon them. In many septic and infective processes, puerperal fever, pyæmia, etc., hæmoglobinæmia occurs. Physiologists now believe, but it is not formally established, that the red blood corpuscles are broken up and converted in the liver into bile pigment. It is supposed that in disease this process is interfered with, the destruction taking place in excess of the power of conversion, or the process stopping short at the stage of destruction.

Paroxysmal Hæmoglobinuria differs essentially from the above. Practically nothing was known of it until twenty years, when Dr. George Harley published two cases under the title of intermittent hæmaturia, and it was almost simultaneously described by Dr. Arthur Hill Hassall as intermittent or winter hæmaturia. Later on Pavy called it paroxysmal hæmaturia. As it came to be recognised that blood colouring matter, and not blood corpuscles, was present in the urine it acquired the name of paroxysmal hæmatinuria, and in 1872 this was changed by Lebert to paroxysmal hæmoglobinuria in consequence of the discovery by Gschleiden that the spectroscope showed the colouring matter to be not hæmatin, but hæmoglobin or methæmoglobin. Mesnet, in 1881, suggested the title of hæmoglobinuria *a frigore*, which suggests its true pathogeny. It is most common in young adults, but affects all ages, and both sexes, although it is very much less common in females. The exciting cause is unquestionably a chill. An interesting apparent exception was published by Rosenbach, in the case of a boy whose attacks were more common in summer than in winter, but it turned out that he was kept in a warm room in the winter, while in summer he was allowed to go out and play. It has often been observed that patients are specially liable to be attacked when, or after, making considerable muscular exertion. Nothing is known definitely about the predisposing causes, except that a history of syphilis has been obtained in some cases and good results have been alleged to follow antisyphilitic treatment in some of these. It is closely allied to Raynaud's disease and is sometimes associated

with it. There is no doubt that the blood corpuscles are broken up during the stasis of the blood in the peripheral parts exposed to cold,—the hands, ears, nose, etc. It has been produced at will, in susceptible persons, by plunging their hands into cold water, and free hæmoglobin may be found in the blood serum (Hayem). The attacks are sometimes preceded by a distinct rigor, or by yawning, formication, or headache; the temperature may fall below normal, in one example as low as 96·1° in the axilla, with lividity of the hands, feet and ears. These premonitory symptoms are followed by lassitude, weakness, pains in the back and limbs, and a desire to make water; on voiding urine the patient is astonished to see that it contains blood. The temperature may rise during the attack to a considerable height; the attack may last a few hours or several days. The skin and conjunctivæ have been observed to become a peculiar dusky colour; some patients have been described as jaundiced. There is often profuse sweating, sometimes confined to certain localities as the forehead or hands.

CASE 89. *Paroxysmal Hæmoglobinuria.*—K. G., aged 28, a labourer, was admitted into hospital on February 22nd, 1886, complaining of shivering, pain in the back and legs, and bloody urine, which had lasted since the previous morning. He had been subject to these attacks for the last three winters; the first came on while working in a cold wind in the early winter of 1881. There was no history of ague or residence in a malarial district. He had had syphilis, a chancre followed by a skin eruption ten years before. He fell from a scaffold in 1879, and had a blow on the head three years ago; but these were not in any way related to his attacks. While in hospital he had a well-marked attack, which I will relate in detail.

On March 4th, his temperature was normal; he passed 40 ounces of urine, which was quite normal in every respect.

March 5th was a clear but very cold day, and he went into the yard between 9 and 10 a.m., for twenty minutes. At 10.30 he began to shiver; temperature 98°. At 10.45 he passed urine, which contained a trace of albumen, and gave a faint hæmoglobin reaction. At 11.0 his temperature was 100°. At 11.15 he passed 2 ounces of urine, which looked like pure blood; this was at once examined microscopically, and showed no blood corpuscles, but a few round cells, much granular matter, granular casts, and oxalates. The spleen was distinctly enlarged, reaching 2 inches below the costal border. 11.30, Temperature 105°; five minutes later he vomited. 12 noon, Temperature 106°; pulse 124; respiration 44. 12.30, Temperature 105°; sweating profusely; complained of rushing noises in his head as soon as he began to get warm, and pain in his back when the attack came on, but these have now left him. 1.0 p.m. Temperature 105°; copious faintly acid sweat; complains again of pain in the back. 2.0, Temperature 104°; urine like tawny port, faintly acid, 1015; deposit under the microscope does not differ from that previously des-

cribed ; tested for indican with HCl and $CaCl_2$ gives a rose pink colour, indigo red. 3.0, Temperature 102° ; pulse 116. 4.0, Temperature 101°. 5.0, Temperature 100°. 6.0, Temperature 100° ; has stopped sweating about half an hour ; no pain in the back ; pulse 88 ; difficulty in commencing to pass water ; urine amber, 1014, faintly acid ; deposits a brownish cloud, which gave the hæmoglobin reaction, and, under the microscope, was composed of granular matter. 6.30, Temperature 99°. 9.0, Temperature 98°. 11.0, Temperature 98·5° ; urine pale amber, 1017 ; deposits a mucous cloud, acid ; gives hæmoglobin reaction.

March 6th.—8.10 a.m. Temperature 98° ; pulse 80 ; urine 1023, acid, amber ; very little granular deposit ; slight reaction with guaiacum ; spleen cannot be felt. The urine passed later in the day contained only a faint trace of albumen ; bowels confined.

March 7th.—Urine free from albumen ; complains of headache ; tongue foul ; bowels open.

He had another slight attack before leaving hospital, and was finally discharged on March 31st, but has been in hospital since.

The next case differs from the preceding in the absence of pyrexia.

CASE 90. *Paroxysmal Hæmoglobinuria.*—J. E., 86, boiler-maker, was admitted into hospital on October 18th, 1886, complaining of chills, and passing bloody urine. He said that thirteen years ago, on a cold day in early winter, he was hard at work, when his feet suddenly became cold, and the next urine he passed contained blood. Since then he has been liable to these attacks every month or three weeks throughout the cold weather. He had never lived further than eight miles away from Birmingham, had never had ague or syphilis, but had drunk a good deal of beer. He was a stoutly-built, florid-complexioned man. Physical signs normal. Temperature on admission 99°, afterwards generally below 98° ; urine 1024, acid, brownish red ; urea 2·6 per cent., contained albumen, hæmoglobin, hyaline casts, yellowish brown granular matter, oxalates, no blood corpuscles. He said that he has occasionally pains in his back preceded by a chill, which commences in his feet and passes upwards ; the muscles of his legs twitch. The chill lasts about two hours, and when he gets warm he passes a large quantity of dark coloured urine, and the pain in his back goes away. He attributed his present attack to getting wet the day before. His conjunctivæ were slightly yellow, and he says when he is very bad his eyes are very yellow. An attempt was made to get some blood serum by means of a blister, but this did not rise. The urine became normal by the 21st, and he left the hospital on November 1st.

The colouring of the conjunctivæ is evidence of free colouring matter in the blood.

The observations in Case 89 made on the urine directly it was passed disprove the statement that blood corpuscles are always present in the urine at that stage; but there is a strong resemblance between these cases and those of hæmaturia due to chill (see Case 87).

It is worth bearing in mind that albuminuria is occasionally persistent in these cases, and Dr. Ralfe believed that this is due

to a permanent inability to dispose of the albuminous material set free by the destruction of the red blood corpuscles. But if this were true, the albumen excreted should be globulin, not serum albumen, a suggestion already made some years ago by Sir William Gull. I have endeavoured to test the truth of this hypothesis, but my analyses always showed that serum albumen was present as well as globulin.

These attacks are not dangerous to life, but end in recovery after a longer or shorter time, and except for some anæmia and the liability to relapse, the patient enjoys good health. In some cases the predisposition ceases abruptly, but in others it persists throughout life, and in one notable case was not benefited even by residence in a tropical climate (Madras). It is doubtful whether remedies have any decided effect, on account of the tendency which the condition has to disappear spontaneously, but Begbie thought scruple doses of chloride of ammonium cured his case. After the attacks the administration of iron is indicated. Susceptible persons should avoid chills by suitable clothing, and when circumstances permit, the winter should be spent in a warm climate.

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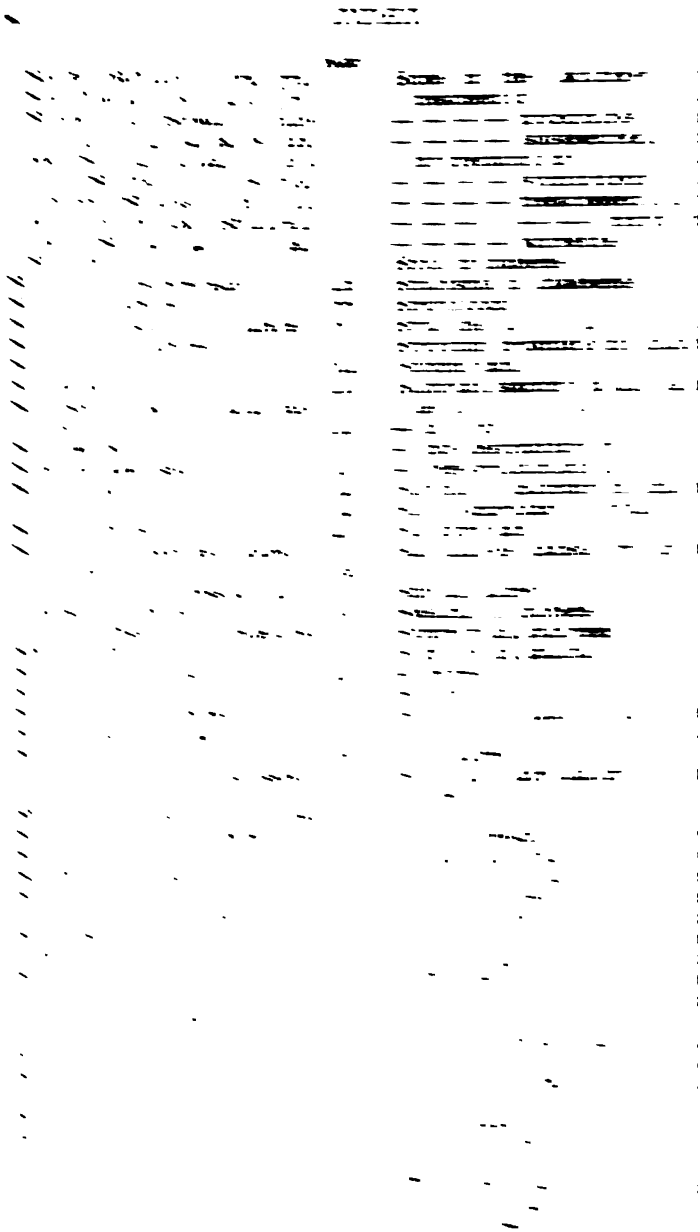

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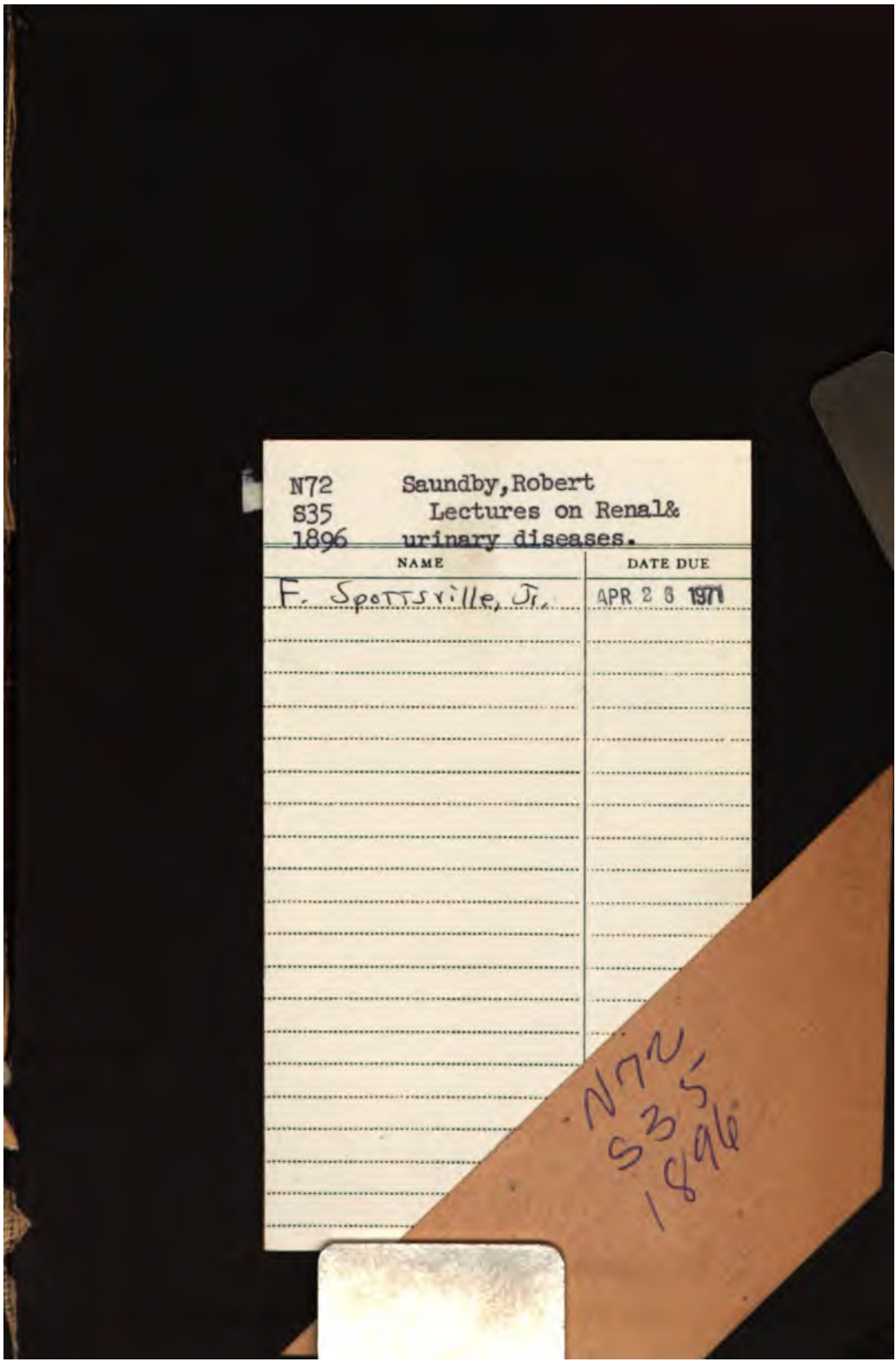
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